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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Apr 08	"Ask CAS" for self-help around the clock
NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27	Oct 21	EVENTLINE has been reloaded
NEWS 28	Oct 24	BEILSTEIN adds new search fields
NEWS 29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS 31	Nov 18	DKILIT has been renamed APOLLIT
NEWS 32	Nov 25	More calculated properties added to REGISTRY
NEWS 33	Dec 02	TIBKAT will be removed from STN
NEWS 34	Dec 04	CSA files on STN
NEWS 35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36	Dec 17	TOXCENTER enhanced with additional content
NEWS 37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 38	Dec 30	ISMEC no longer available
NEWS 39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS 41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC

NEWS EXPRESS	January 6 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

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Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09560711.str

L1 STRUCTURE UPLOADED

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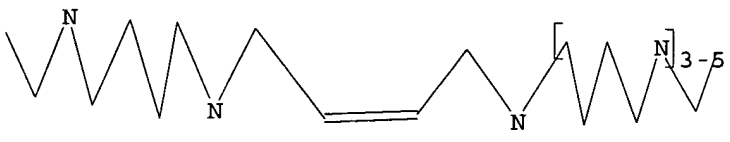

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED -     96 TO ITERATE

100.0% PROCESSED      96 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:         1333 TO     2507
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

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FULL SCREEN SEARCH COMPLETED -   2348 TO ITERATE

100.0% PROCESSED    2348 ITERATIONS                               8 ANSWERS
SEARCH TIME: 00.00.01

L3            8 SEA SSS FUL L1

=> fil caplus
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                                                   ENTRY    SESSION
FULL ESTIMATED COST                               148.15     148.36

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FILE COVERS 1907 - 6 Feb 2003  VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003  (20030205/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l3
L4            6 L3

=> d l4 1-6 abs ibib hitstr
```

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB Polyamine or polyamine analog-amino acid conjugates (M)-N(E)-(B-A-B-NH)4-E or (M)-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [M is an amino acid; A is a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B is a bond, alkyl, or alkenyl; E is H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl], including salts or stereoisomers, were prepd. for use as antiviral agents.

An example is the polyamine glutamine conjugate SL-11165 [NH2CH(CH2CH2CONH2)CON(Et)(CH2CH2CH2CH2NH)4Et.bul.5HCl]. Thus, (E)-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NHEt was prepd. by a multi-step sequence starting from 4-bromobutanenitrile, N-(mesitylsulfonyl)ethanamine, and (E)-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:888472 CAPLUS
DOCUMENT NUMBER: 137:384565
TITLE: Preparation of polyamine or polyamine analog-amino acid conjugates as antiviral agents
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.; Gutierrez, Jesus A.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA; Eli Lilly & Company
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002091989	A2	20021121	WO 2001-US43887	20011108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-246804P P 20001108
OTHER SOURCE(S): MARPAT 137:384565

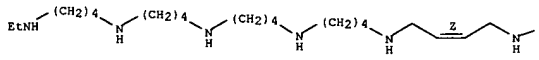
IT **304911-08-8P**, SL 11150
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)

RN 304911-08-8 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

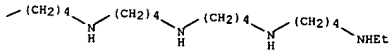
L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A



●10 HCl

PAGE 1-B



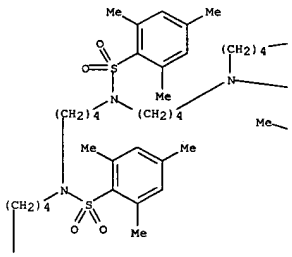
IT **304863-19-2P 304863-21-6P 304911-07-7P**, SL 11144
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)

RN 304863-19-2 CAPLUS
CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A



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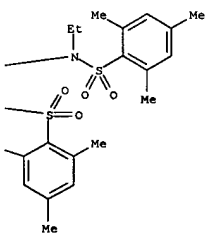
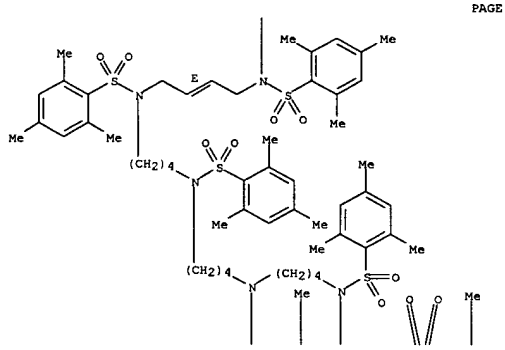


L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



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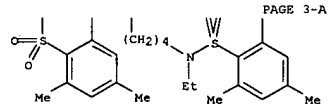
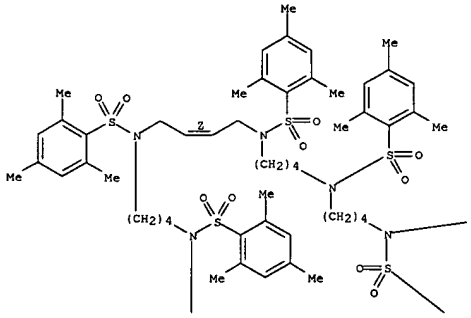


RN 304863-21-6 CAPLUS
CN Benzenesulfonamide, N,N'-(2Z)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A



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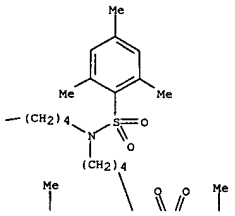
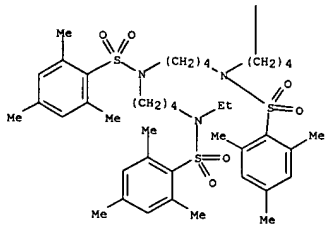


L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



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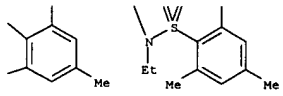
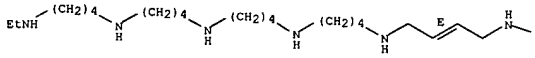


RN 304911-07-7 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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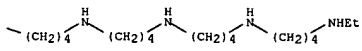


L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB Conjugates of polyamines analogs conjugated to at least one amino acid of formula M-N(E)-(B-A-B-NH)4-E or M-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [wherein M = independently an amino acid, esp. glutamine, asparagine, lysine, ornithine, arginine, histidine, or citrulline; A = independently a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B = independently a bond, alkyl, or alkenyl; E = independently H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; and salts or stereoisomers thereof] were tested and claimed for pharmaceutical use as anticancer agents. For example, the polyamine glutamine conjugate SL-11165 [NH2CH(CH2CH2CONH2)CON(Et)(CH2CH2CH2CH2NH)4Et.bul.5HCl] exhibited ID50 values of >31.65, 4.1, and >31.25 against the DuPro, PC-3, and LnCap prostate cancer cell lines, resp. In addn., conformationally restricted polyamine analogs were prepd. Thus, {E}-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NH Et was prepd. in a multi-step sequence starting from 4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:368258 CAPLUS
DOCUMENT NUMBER: 136:386292
TITLE: Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as anticancer agents
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038105	A2	20020516	WO 2001-US43585	20011108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002035126	A5	20020521	AU 2002-35126	20011108
PRIORITY APPLN. INFO.:			US 2000-246804P P	20001108
			WO 2001-US43585 W	20011108

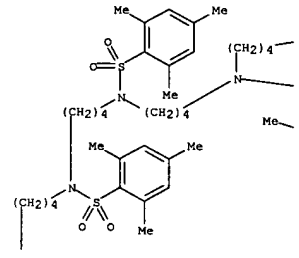
OTHER SOURCE(S): MARPAT 136:386292
IT **304863-19-2P**, Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- **304863-21-6P**, Benzenesulfonamide, N,N'-(2Z)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- **304911-07-7P**, SL 11144
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of conformationally restricted polyamines and use

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
of polyamine amino acid conjugates as anticancer agents)

RN 304863-19-2 CAPLUS
CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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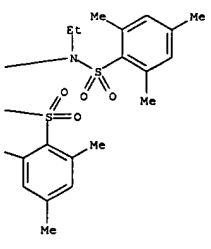

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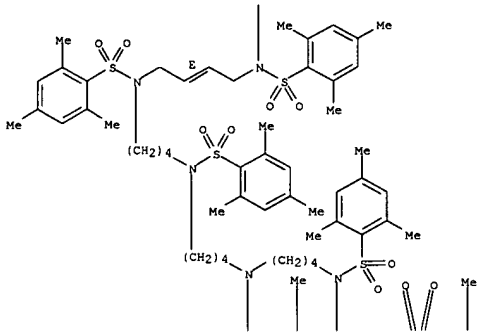

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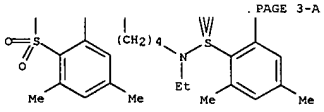

RN 304863-21-6 CAPLUS
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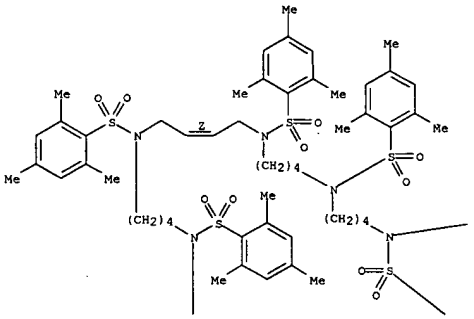
Double bond geometry as shown.

PAGE 1-A



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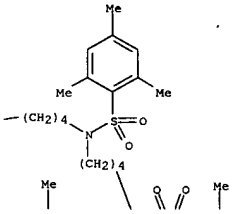

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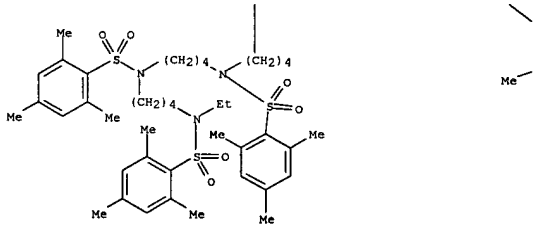
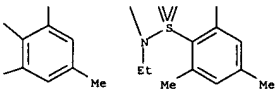


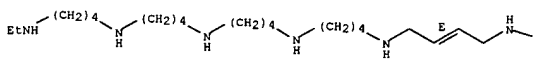
PAGE 2-B



RN 304911-07-7 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

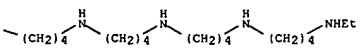
Double bond geometry as shown.

PAGE 1-A



●10 HCl

PAGE 1-B



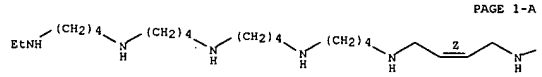
IT **304911-08-8P**, SL 11150
RL: SPN (Synthetic preparation); PREP (Preparation)
(polyamine; prepn. of conformationally restricted polyamines and use of

polyamine amino acid conjugates as anticancer agents)

RN 304911-08-8 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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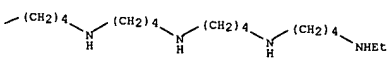


L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB The pre-emergent spore stages of Encephalitozoon cuniculi were evaluated for polyamine uptake and interconversion. The possible effects of SL-11158 on polyamine metab. were also studied. Enc. cuniculi was maintained on RK-13 cells, which were grown to 80% confluency in Corning T-26 or Falcon T-75 flasks and infected with 5 x 105 spores. Enc. cuniculi assimilated and interconverted polyamines; spermidine was taken up far more readily than spermine. A large proportion of the metabolites were excreted as in mammalian cells. The major effects of polyamine analogs on cells include competition for uptake through polyamine transporters, upregulation of spermidine/spermine N1-acetyltransferase, and excretion of polyamines, leading to redn. of polyamine content. The inhibition of metabolite prodn. and excretion by a low concn. of SL-11158 suggested that this polyamine analog targets, in part, polyamine interconversion in this parasite.

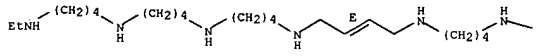
ACCESSION NUMBER: 2002:277765 CAPLUS
DOCUMENT NUMBER: 137:182043
TITLE: SL-11158, a synthetic oligoamine, inhibits polyamine metabolism of Encephalitozoon cuniculi
AUTHOR(S): Bacchi, Cyrus J.; Orozco, Daniel; Weiss, Louis M.; Frydman, Benjamin; Valasinas, Aldonia; Yarlett, Nigel; Marton, Laurence J.; Wittner, Murray
CORPORATE SOURCE: Haskins Laboratories, Pace University, New York, NY, 10038, USA
SOURCE: Journal of Eukaryotic Microbiology (2001), (Suppl.), 92S-94S
CODEN: JEMIED; ISSN: 1066-5234
PUBLISHER: Society of Protozoologists
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **412351-17-8**, SL-11158
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthetic oligoamine SL-11158 inhibits polyamine metab. of Encephalitozoon cuniculi)

RN 412351-17-8 CAPLUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (17E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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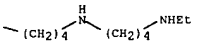


REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB Microsporidia are eukaryotic obligate intracellular protists that are emerging pathogens in immunocompromised hosts, such as patients with AIDS or patients who have undergone organ transplantation. We have demonstrated in vitro and in vivo that synthetic polyamine analogs are effective antimicrosporidial agents with a broad therapeutic window. CD8-knockout mice or nude mice infected with the microsporidian Encephalitozoon cuniculi were cured when they were treated with four different novel polyamine analogs at doses ranging from 1.25 to 5 mg/kg of body wt./day for a total of 10 days. Cured animals demonstrated no evidence of parasitemia by either PCR or histol. staining of tissues 30 days after untreated control animals died.

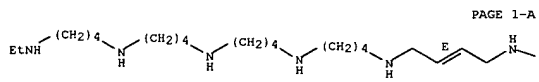
ACCESSION NUMBER: 2002:30291 CAPLUS
DOCUMENT NUMBER: 136:318859
TITLE: Novel synthetic polyamines are effective in the treatment of experimental microsporidiosis, an opportunistic AIDS-associated infection
AUTHOR(S): Bacchi, Cyrus J.; Weiss, Louis M.; Lane, Schenella; Frydman, Benjamin; Valasinas, Aldonia; Reddy, Venodhar; Sun, Jerry S.; Marton, Laurence J.; Khan, Imitiaz A.; Moretto, Magali; Yarlett, Nigel; Wittner, Murray
CORPORATE SOURCE: Haskins Laboratories and Departments of Biology and Chemistry, Pace University, New York, NY, 10038-1598, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(1), 55-61
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **304911-07-7**, SL 11144
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11144; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-07-7 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

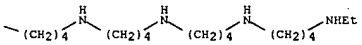
Double bond geometry as shown.

PAGE 1-A



●10 HCl

PAGE 1-B



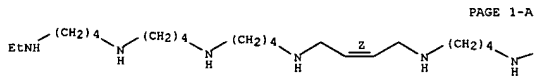
L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

IT **412351-16-7**, SL 11157 **412351-17-8**, SL 11158
412351-20-3, SL 11172
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

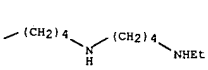
RN 412351-16-7 CAPLUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



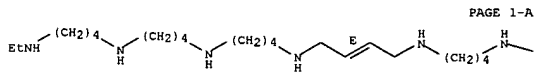
PAGE 1-B



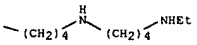
RN 412351-17-8 CAPLUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (17E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

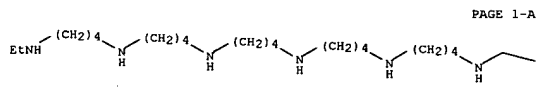


RN 412351-20-3 CAPLUS
CN 5,10,15,20,25,30,35,40,45,50-Decaaza-27-tetrapentacontene-1,54-diamine, N,N'-diethyl-, (27E)- (9CI) (CA INDEX NAME)

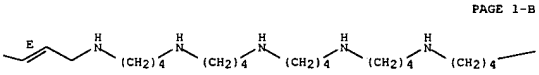
Double bond geometry as shown.

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A



PAGE 1-B



PAGE 1-C

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB Novel conformationally restricted polyamines, such as E-NH-(B-A-B-NH)4-E [A, E = bond, alkyl, alkenyl, alkynyl, cycloalkyl, cycloaryl, cycloalkenyl; B = bond, alkyl, alkenyl], were prepd. for pharmaceutical use as anticancer agents. Thus, (E)-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NHEt was prepd. in a multistep sequence starting from mesityl chloride 4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol. The prepd. polyamines were tested for antiproliferative activity against human prostate cancer cell lines, such as PC3 and DUPRO.

ACCESSION NUMBER: 2000:790505 CAPLUS
DOCUMENT NUMBER: 133:350095
TITLE: Preparation of conformationally restricted polyamine analogs as disease therapies
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Reddy, Venodhar K.; Valasinas, Aldonia; Blokhin, Andrei V.; Basu, Hirak S.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066587	A2	20001109	WO 2000-US11591	20000427
WO 2000066587	A3	20010125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1177197	A2	20020206	EP 2000-928583	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010701	A	20020213	BR 2000-10701	20000427
JP 2002543202	T2	20021217	JP 2000-615617	20000427
PRIORITY APPLN. INFO.:			US 1999-131779P P	19990430
			WO 2000-US11591 W	20000427

OTHER SOURCE(S): MARPAT 133:350095

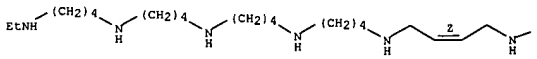
IT **304863-62-5P 304911-08-8P**, SL 11150
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of conformationally restricted polyamines as antiproliferative prostate cancer agents)

RN 304863-62-5 CAPLUS
CN 3,8,13,18,23,28,33,38,43,48-Decaazapentacont-25-en-1-ol, decahydrochloride, (25Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A



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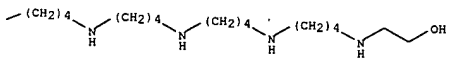
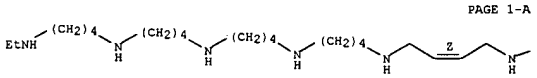
PAGE 1-B



RN 304911-08-8 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22Z)- (9CI) (CA INDEX NAME)

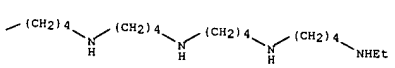
Double bond geometry as shown.

PAGE 1-A



●10 HCl

PAGE 1-B



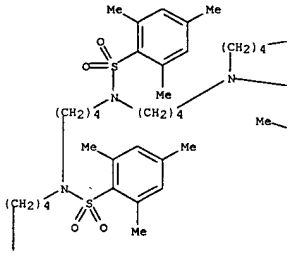
IT **304863-19-2P 304863-21-6P 304911-07-7P**, SL 11144
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of conformationally restricted polyamines as antiproliferative prostate cancer agents)

RN 304863-19-2 CAPLUS
CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

Double bond geometry as shown.

PAGE 1-A



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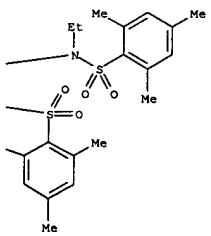
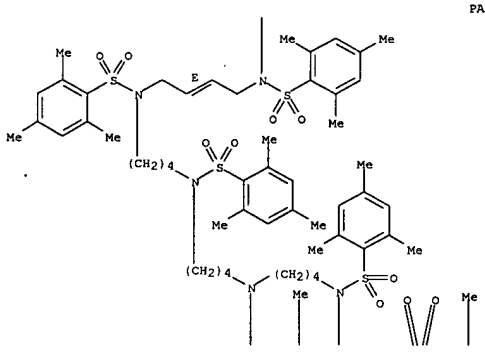
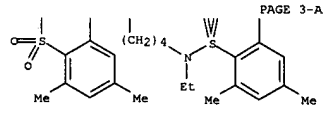


L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



PAGE 3-A

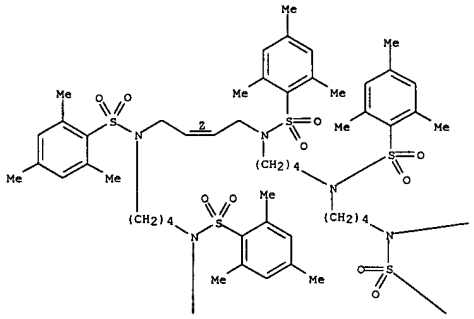


RN 304863-21-6 CAPLUS
CN Benzenesulfonamide, N,N'-(2Z)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

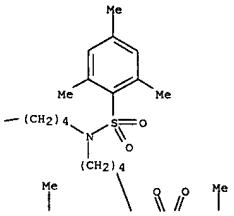
Double bond geometry as shown.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A

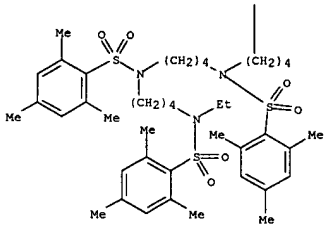


PAGE 1-B

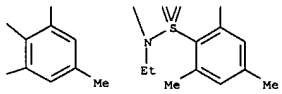


L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



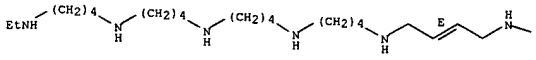
PAGE 2-B



RN 304911-07-7 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

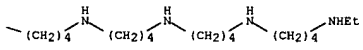
Double bond geometry as shown.

PAGE 1-A



●10 HCl

PAGE 1-B



L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS

AB The invention relates to peptide conjugates in which cytocidal and cytostatic agents, such as polyamine analogs or naphthoquinones, are conjugated to a polypeptide recognized and cleaved by enzymes such as prostate-specific antigen (PSA) and cathepsin B. Methods of using these conjugates in the treatment of prostate diseases are also provided. Thus, C2[CH2NH(CH2)4NHEt]2.4HCl (SL-11103), 4-[[7-[4-(9-acridinylamino)phenyl]heptyl]oxy]-1,2-naphthoquinone (SL-11064), and morpholino-Ser-Lys-Leu-Gln-.beta.-Ala-.beta.-lapachone (SL-11147) were prepd. and assayed for antitumor activity against human prostate cancer cell lines, such as PC-3 and DUPRO.

ACCESSION NUMBER: 2000:790358 CAPLUS
DOCUMENT NUMBER: 133:350515
TITLE: Preparation of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066175	A2	20001109	WO 2000-US11542	20000427
WO 2000066175	A3	20010802		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173223	A2	20020123	EP 2000-928565	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010700	A	20020213	BR 2000-10700	20000427
JP 2002543163	T2	20021217	JP 2000-615058	20000427
PRIORITY APPLN. INFO.:			US 1999-131809P P	19990430
			WO 2000-US11542 W	20000427

OTHER SOURCE(S): MARPAT 133:350515

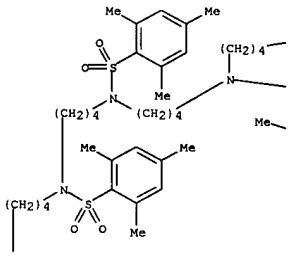
IT **304863-19-2P 304863-21-6P 304911-07-7P 304911-08-8P**, SL 11150
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)

RN 304863-19-2 CAPLUS
CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

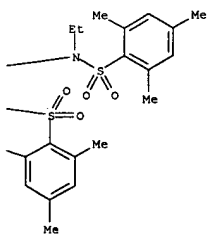
Double bond geometry as shown.

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A

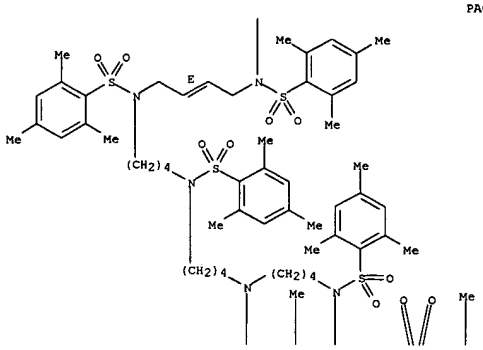


PAGE 1-B



L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



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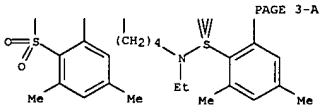
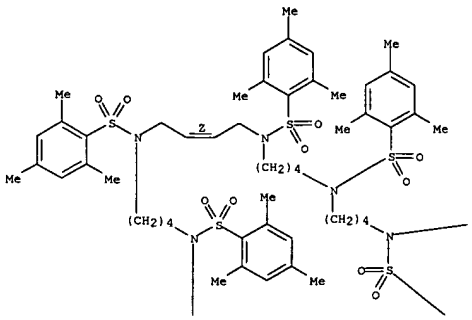


RN 304863-21-6 CAPLUS
CN Benzenesulfonamide, N,N'-(2Z)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-A



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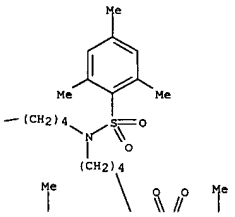
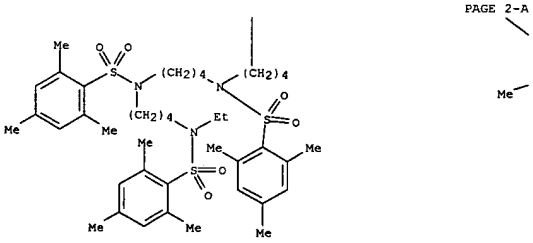


L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



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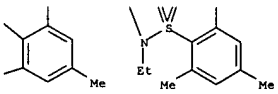
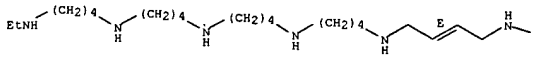


RN 304911-07-7 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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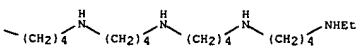
PAGE 1-B

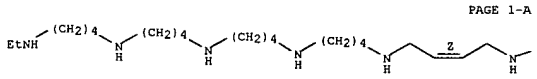


RN 304911-08-8 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22Z)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

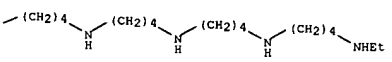
Double bond geometry as shown.

PAGE 1-A



●10 HCl

PAGE 1-B



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FULL ESTIMATED COST                                    29.72     178.08

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                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -3.91      -3.91

FILE 'REGISTRY' ENTERED AT 16:22:34 ON 06 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    5 FEB 2003  HIGHEST RN 486392-61-4
DICTIONARY FILE UPDATES:   5 FEB 2003  HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
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100.0% PROCESSED      13 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           44 TO      476
PROJECTED ANSWERS:               1 TO       80

L6            1 SEA SSS SAM L5

=> s l5 full
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FULL SCREEN SEARCH COMPLETED -    238 TO ITERATE

100.0% PROCESSED     238 ITERATIONS                              28 ANSWERS
SEARCH TIME: 00.00.01

L7            28 SEA SSS FUL L5

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
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FULL ESTIMATED COST                              149.35     327.43

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE      TOTAL
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L8 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB The invention is a series of novel and effective inhibitors of integrase, an essential in the life cycle of retroviruses. These compds. were designed to have a restricted conformation for the detn. of the integrase binding site and mechanism of inhibition. The integrase inhibitors of the invention are effective in the submicromolar range, and thereby provide novel lead compds. for the development of anti-viral therapeutics.

ACCESSION NUMBER: 2002:31406 CAPLUS
DOCUMENT NUMBER: 136:79737
TITLE: Symmetric inhibitors of HIV integrase, mammalian topoisomerase and serineprotease
INVENTOR(S): Harrison, Robert W.; Skalka, Anna Marie
PATENT ASSIGNEE(S): Thomas Jefferson University, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

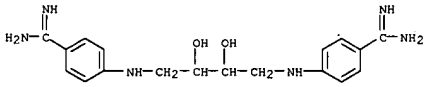
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002516	A2	20020110	WO 2001-US19923	20010622
WO 2002002516	A3	20021024		

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-215474P P 20000630

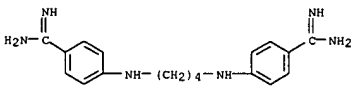
IT **387397-93-5P**, RWH 23
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(sym. inhibitors of HIV integrase, mammalian topoisomerase and serineprotease)

RN 387397-93-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-[(2,3-dihydroxy-1,4-butanediyl)diimino]bis- (9CI) (CA INDEX NAME)

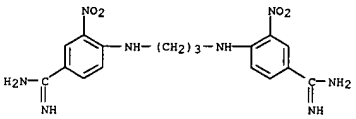


L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

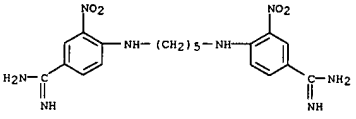
RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)



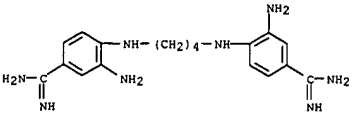
RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-89-9 CAPLUS

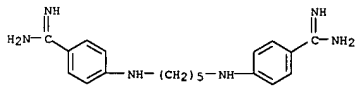
L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB A proposed model for the interaction of bisamidine analogs with the B-DNA receptor is established by structure-property relationship studies derived from 3D-WHIM descriptor calcns. Three classes, each with relevant information about structural relationships, were detd. by PCA and SIMCA analyses for mol. conformations described by 3D-WHIM descriptors for a set of 29 bisamidines with antileishmaniasis and anti-PCP activities. Shape, distribution and dimension properties mostly govern the interaction of bisamidines with B-DNA through the minor groove AT rich regions.

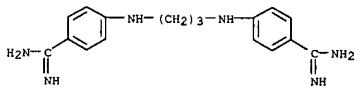
ACCESSION NUMBER: 2000:664385 CAPLUS
DOCUMENT NUMBER: 133:344182
TITLE: 3D-WHIM pattern recognition study for bisamidines. A structure-property relationship study
AUTHOR(S): Menezes, Fabiano A. S.; Montanari, Carlos A.; Bruns, Roy E.
CORPORATE SOURCE: Departamento de Quimica, Universidade Federal de Minas Gerais, Belo Horizonte, 31270-901, Brazil
SOURCE: Journal of the Brazilian Chemical Society (2000), 11(4), 393-397
CODEN: JOCSET; ISSN: 0103-5053
PUBLISHER: Sociedade Brasileira de Quimica
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **124076-63-7 125880-81-1 125880-82-2 125880-83-3 125880-84-4 125880-86-6 125880-89-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(3D-WHIM pattern recognition and structure-activity relationship study for bisamidines)

RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

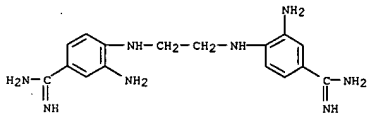


RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS

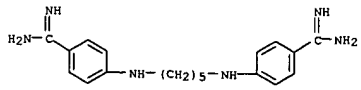
AB Arom. dicationic drugs have a broad spectrum of activity against protozoal and fungal pathogens including Pneumocystis carinii, Leishmania mexicana amazonensis, Cryptosporidium parvum, and Cryptococcus neoformans. Pentamidine serves as the exemplar for an extensive collection of newly synthesized related compds., which have reduced toxicity and a wider range of target organisms. Assays of pentamidine and related compds. have depended on HPLC-tandem mass spectrometry (HPLC-TMS) for the quantitation and identification of drug and metabolites. Immunoassays for pentamidine would have many advantages over the HPLC methods including relative simplicity of assay format and required equipment, convenience in sample prepn. and redn. in time and cost of assays. In this report the authors describe a simple ELISA based immunoassay for pentamidine and pentamidine-like drugs with requisite sensitivity and specificity for use as a clin. assay (EC50 value of about 50 nanomolar). Immunogen was synthesized by coupling the hapten aminopentamidine to ovalbumin (chem. modified to provide an optimal no. of -SH groups) using sulfo-MBS. Maleic-anhydride activated ELISA plates were covalently sensitized using the amino-pentamidine hapten and used in an inhibitory ELISA assay format whereby the ability of analyte to suppress antibody binding to sensitized plate was measured. The assay detects primarily the phenolic amidine of pentamidine when in a para position and hence can also detect structurally related derivs. of pentamidine of potential interest as new therapeutic agents.

ACCESSION NUMBER: 2000:204083 CAPLUS
DOCUMENT NUMBER: 133:114510
TITLE: Immunoassays for pentamidine and related compounds: development of a facile inhibitory ELISA suitable for clinical use
AUTHOR(S): Reisner, Howard M.; Gray, Danny R.; Jones, Susan K.; Rose, Beate G.; Tidwell, Richard R.
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599-7525, USA
SOURCE: Journal of Clinical Laboratory Analysis (2000), 14(2), 73-82
CODEN: JCANEM; ISSN: 0887-8013
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **124076-63-7**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(immunoassays for pentamidine and related compds.)

RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

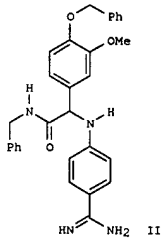
L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS

GI



II

AB RR1NCOCHR2NH2C(:NG1)NHG2 [I; 1 of G1,G2 = H and the other = H, OH, alkyl, alkoxy, etc.; R = (un)substituted alkyl, cycloalkyl, aryl; R1 = H or alkyl; R2 = (un)substituted Ph or -pyridyl; Z = (3-hydroxy)1,4-phenylene] were prepd. Thus, 3,4-(MeO)(PhCH2O)C6H3CHO, 4-(H2N)C6H4C(:NH)NH2, and PhCH2NC were condensed to give, after acidification, title compd. II.HCl. Data for biol. activity of I were given.

ACCESSION NUMBER: 1999:375282 CAPLUS
DOCUMENT NUMBER: 131:44656
TITLE: Preparation of N-(4-amidinophenyl)phenylglycineamides as factor VIIa/tissue factor inhibitors
INVENTOR(S): Grobke, Katrin; Ji, Yu-hua; Wallbaum, Sabine; Weber, Lutz
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 921116	A1	19990609	EP 1998-122169	19981126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6140353	A	20001031	US 1998-204373	19981202
ZA 9811077	A	19990604	ZA 1998-11077	19981203
NO 9805646	A	19990607	NO 1998-5646	19981203
AU 9895210	A1	19990624	AU 1998-95210	19981203
AU 739769	B2	20011018		
CN 1224714	A	19990804	CN 1998-126979	19981204
JP 11246507	A2	19990914	JP 1998-345875	19981204
JP 3236267	B2	20011210		
BR 9805320	A	20000411	BR 1998-5320	19981204

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

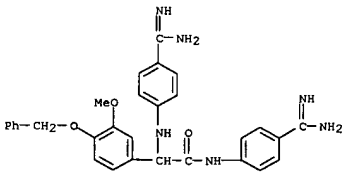
PRIORITY APPLN. INFO.: EP 1997-121285 A 19971204
EP 1998-121374 A 19981110
OTHER SOURCE(S): MARPAT 131:44656

IT **227021-08-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(4-amidinophenyl)phenylglycineamides as factor VIIa/tissue factor inhibitors)

RN 227021-08-1 CAPLUS
CN Benzeneacetamide, N-[4-(aminoiminomethyl)phenyl]-.alpha.-[[4-(aminoiminomethyl)phenyl]amino]-3-methoxy-4-(phenylmethoxy)-, acetate (9CI) (CA INDEX NAME)

CM 1

CRN 227021-07-0
CMF C30 H30 N6 O3



CM 2

CRN 64-19-7
CMF C2 H4 O2

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

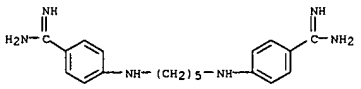
L8 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

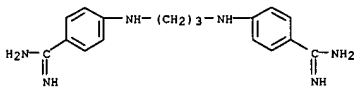
AB Twenty analogs of pentamidine (including I), 7 primary metabolites of pentamidine, and 30 dicationic substituted bisbenzimidazoles were screened for their inhibitory and fungicidal activities against Candida albicans and Cryptococcus neoformans. A majority of the compds. had MICs at which 80% of the strains were inhibited (MIC80s) comparable to those of amphotericin B and fluconazole. Unlike fluconazole, many of these compds., such as II and III, were found to have potent fungicidal activity. The most potent compd. against C. albicans had an MIC80 of .ltoreq.0.09 .mu.g/mL, and the most potent compd. against C. neoformans had an MIC80 of 0.19 .mu.g/mL. Selected compds., such as IV, were also found to be active against Aspergillus fumigatus, Fusarium solani, Candida species other than C. albicans, and fluconazole-resistant strains of C. albicans and C. neoformans. It is clear from the data presented here that further studies on the structure-activity relationships, mechanisms of action and toxicities, and in vivo efficacies of these compds. are warranted to det. their clin. potential.

ACCESSION NUMBER: 1998:664985 CAPLUS
DOCUMENT NUMBER: 130:22732
TITLE: Structure-in vitro activity relationships of pentamidine analogs and dication-substituted bis-benzimidazoles as new antifungal agents
AUTHOR(S): Del Poeta, Maurizio; Schell, Wiley A.; Dykstra, Christine C.; Jones, Susan; Tidwell, Richard R.; Czarny, Agnieszka; Bajic, Miroslav; Bajic, Marina; Kumar, Arvind; Boykin, David; Perfect, John R.
CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(10), 2495-2502
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7 125880-81-1 125880-83-3 125880-85-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-in vitro activity relationships of pentamidine analogs and dication-substituted bis-benzimidazoles as new antifungal agents)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

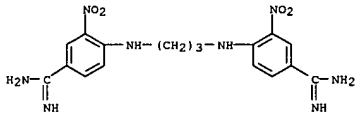
L8 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



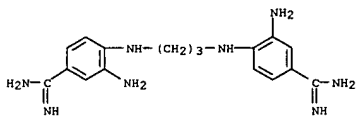
RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

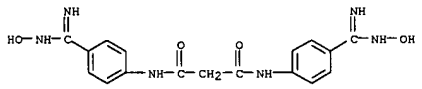


REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

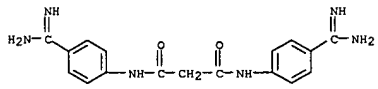
L8 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS
AB Arom. dicationic compds., such as pentamidine, have potent antimicrobial activities. Clin. use of these compds. has been restricted, however, by their toxicity and limited oral activity. A novel approach, using amidoxime derivs. as prodrugs, has recently been proposed to overcome these limitations. Although results were presented for amidoxime derivs. of only one diamidine, pentamidine, the authors in the original proposal claimed that amidoxime derivs. would work as effective prodrugs for all pharmacol. active diamidines. Nine novel amidoxime derivs. were synthesized and tested in the present study for activity against Pneumocystis carinii in corticosteroid-suppressed rats. Only three of the nine compds. had significant oral anti-Pneumocystis activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had excellent oral and i.v. activities and reduced acute host toxicity. These compds. are not likely candidates for future drug development, however, because they have chronic toxic effects and the active amidine compds. have multiple sites susceptible to oxidative metab., which complicates their pharmacol. and toxicol. Novel diamidoximes from three other structural classes, contg. different groups linking the cationic moieties, lacked significant oral or i.v. anti-Pneumocystis activity, even though the corresponding diamidines were very active i.v. Both active and inactive amidoximes were readily metabolized to the corresponding amidines by cell-free liver homogenates. Thus, the amidoxime prodrug approach may provide a strategy to exploit the potent antimicrobial and other pharmacol. activities of selected, but certainly not all, arom. diamidines.

ACCESSION NUMBER: 1998:189774 CAPLUS
DOCUMENT NUMBER: 128:303628
TITLE: Anti-Pneumocystis activities of aromatic diamidoxime prodrugs
AUTHOR(S): Hall, James Edwin; Kerrigan, John E.; Ramachandran, Kishore; Bender, Brendan C.; Stanko, Jason P.; Jones, Susan K.; Patrick, Donald A.; Tidwell, Richard R.
CORPORATE SOURCE: Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(3), 666-674
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **206532-33-4P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(anti-Pneumocystis activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)
RN 206532-33-4 CAPLUS
CN Propanediamide, N,N'-bis[4-[(hydroxyamino)iminomethyl]phenyl]- (9CI) (CA INDEX NAME)

L8 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



IT **206532-34-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-Pneumocystis activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)
RN 206532-34-5 CAPLUS
CN Propanediamide, N,N'-bis[4-(aminoiminomethyl)phenyl]- (9CI) (CA INDEX NAME)

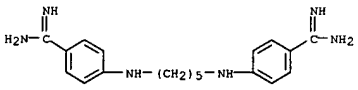


L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB Results are presented for a QSAR anal. of bisamidines, using a similarity index as descriptor. The method allows for differences in conformation of bisamidines at the receptor site to be taken into consideration. In particular, it has been suggested by others that pentamidine binds in the minor groove of DNA in a so-called isohelical conformation, and the authors QSAR supports this suggestion. The mol. similarity index for comparison of mols. can be used as a parameter for correlating and hence rationalizing the activity as well as suggesting the design of bioactive mols. The studied compds. had been evaluated for potency against Leishmania mexicana amazonensis, and this potency was used as a dependent variable in a series of QSAR analyses. For the calcn. of similarity indexes, each analog was in turn superimposed on a chosen lead compd. in a ref. conformation, either extended or isohelical, maximizing overlap and hence similarity by flexible fitting.

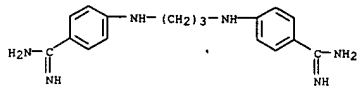
ACCESSION NUMBER: 1996:162810 CAPLUS
DOCUMENT NUMBER: 124:277974
TITLE: Determination of receptor-bound drug conformations by QSAR using flexible fitting to derive a molecular similarity index
AUTHOR(S): Montanari, C. A.; Tute, M. S.; Beezer, A. E.; Mitchell, J. C.
CORPORATE SOURCE: Chem. Lab., Univ. Kent, Canterbury, Kent, CT2 7NH, UK
SOURCE: Journal of Computer-Aided Molecular Design (1996), 10(1), 67-73
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: ESCOM
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7 125880-81-1 125880-82-2 125880-83-3 125880-84-4 125880-86-6 125880-87-7 125880-89-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detn. of receptor-bound drug conformations on DNA by QSAR using flexible fitting to derive a mol. similarity index using bisamidines as Leishmania inhibitors)

RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

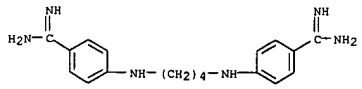


RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)

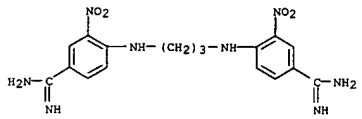
L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



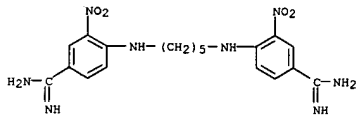
RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

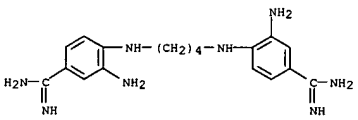


RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

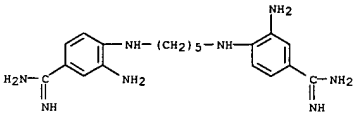


RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

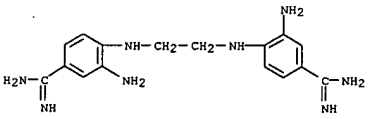
L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

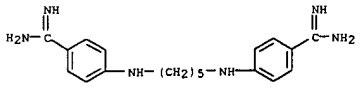


L8 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB The in vitro culture system is described in which Trypanosoma brucei rhodesiense (LOUTat.1) was grown with the human feed layer cell HL-60. The use of this system in detg. the 50% growth Inhibitory Concn. (IC50) of unknown compds. for both the trypanosomes and the host cell was demonstrated. The data shows that several analogs of pentamidine have significantly reduced host cell toxicity but maintain or have increased trypanocidal activity. The value of the trypanosome/HL-60 in vitro culture system as a rapid primary in vitro drug screen is discussed. Based upon the ability of this primary screen to predict potential drug efficacy, several analogs screened in vitro were then tested in vivo. The results of the in vivo tests confirmed the ability of the in vitro screen to predict drug efficacy, and also suggests that better analogs of pentamidine (less host toxicity and greater trypanocidal activity) can be obtained to treat human trypanosomiasis.

ACCESSION NUMBER: 1996:138520 CAPLUS
DOCUMENT NUMBER: 124:249761
TITLE: The in vitro HL-60 cell - Trypanosoma brucei rhodesiense culture system: A rapid in vitro drug screen
AUTHOR(S): Keku, T. O.; Seed, J. R.; Tidwell, R. R.
CORPORATE SOURCE: Department of Medicine, University North Carolina, Chapel Hill, NC, USA
SOURCE: Tropical Medicine and Parasitology (1995), 46(4), 258-62
CODEN: TMPAEY; ISSN: 0177-2392
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in vitro HL-60 cell-Trypanosoma brucei rhodesiense culture system for rapid in vitro trypanocidal drug screening)

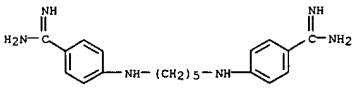
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB A mol. mechanics and mol. dynamics approach has been used to examine the structure of the complex formed between pentamidine and the d(CGCGAATTCGCG)2 duplex. Similar energy calcns. have also been performed on complexes with closely related pentamidine analogs, using the complex with the parent drug as the starting point. The resulting structures of the drug-DNA complexes and their energetics have been examd. and are compared with the reported DNA binding affinities. These studies provide rationalizations for the differences in binding behavior of pentamidine analogs with differing linker chain lengths and arom. ring substitutions.

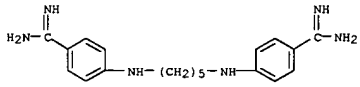
ACCESSION NUMBER: 1993:573590 CAPLUS
DOCUMENT NUMBER: 119:173590
TITLE: DNA minor groove recognition properties of pentamidine and its analogs: A molecular modeling study
AUTHOR(S): Greenidge, Paulette A.; Jenkins, Terence C.; Neidle, Stephen
CORPORATE SOURCE: Cancer Res. Campaign Biomol. Struct. Unit, Inst. Cancer Res., Sutton/Surrey, SM2 5NG, UK
SOURCE: Molecular Pharmacology (1993), 43(6), 982-8
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7**
RL: BIOL (Biological study)
(DNA minor groove recognition properties of, anti-Pneumocysis carinii activity in relation to)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB We have investigated the interactions of six analogs of pentamidine with the N-methyl-D-aspartate (NMDA) receptor complex. All six compds. were effective NMDA receptor antagonists based upon their ability to inhibit [3H]dizocilpine binding to rat brain membranes. IC50 values ranged from 2 to 18 .mu.M, and all compds. had Hill coeffs. in excess of 1 suggesting a non-competitive interaction with [3H]dizocilpine. All compds. also inhibited NMDA- and glycine-induced intracellular Ca2+ changes measured in cultured rat forebrain neurons using the fluorescent indicator, fura-2. IC50 values in this assay ranged from 0.4 to 4.7 .mu.M. Whereas pentamidine is directly toxic to cultured neurons, this was not a consistent finding with the pentamidine analogs tested, indicating that the toxic effects are not related to NMDA receptor antagonism. Finally, all of the agents tested were also effective in protecting neurons from NMDA-induced neurotoxicity. These data emphasize the possible utility of pentamidine-like drugs as neuroprotective agents and suggest that it is possible to generate compds. with a wider margin of safety than pentamidine itself.

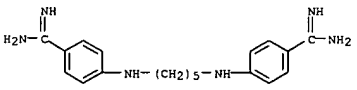
ACCESSION NUMBER: 1993:160558 CAPLUS
DOCUMENT NUMBER: 118:160558
TITLE: Studies on the effects of several pentamidine analogs on the NMDA receptor
AUTHOR(S): Reynolds, Ian J.; Zeleski, Diane M.; Rothermund, Kristi D.; Hartnett, Karen A.; Tidwell, Richard; Aizenman, Elias
CORPORATE SOURCE: Dep. Pharmacol., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1993), 244(2), 175-9
CODEN: EJPPET; ISSN: 0922-4106
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7**
RL: BIOL (Biological study)
(NMDA receptor antagonism by, neurotoxicity and neuroprotective activity in relation to)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB The error of omitting the supplementary material available paragraph has been cor. The error was not reflected in the abstr. or the index entries.

ACCESSION NUMBER: 1993:51883 CAPLUS
DOCUMENT NUMBER: 118:51883
TITLE: Structure and DNA binding activity of analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine). [Erratum to document cited in CA116(9):75694b]
AUTHOR(S): Cory, Michael; Tidwell, Richard R.; Fairley, Terri A.
CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(25), 4767
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7 125880-81-1 125880-82-2**
125880-83-3 125880-84-4 125880-85-5
125880-86-6 125880-87-7 125880-89-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-binding activity of (Erratum))
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-81-1 CAPLUS
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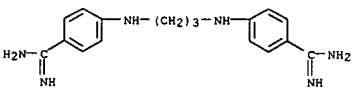
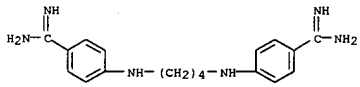
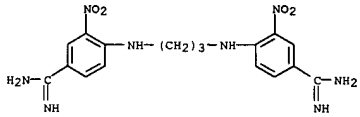


RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

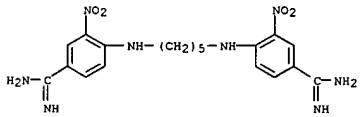
L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



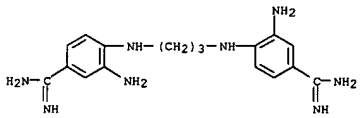
RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

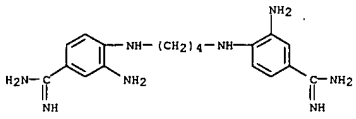


RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

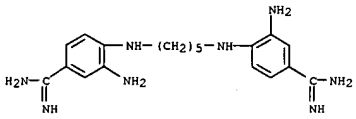


RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

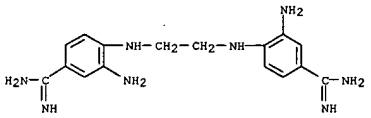
L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

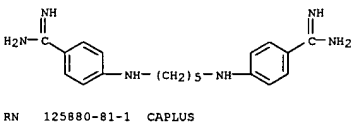


L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS

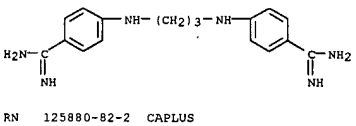
AB The DNA binding properties of a series of bisbenzamidines related to the clin. used antipneumocystis drug pentamidine (I) were studied. Changes in the thermal denaturation temp. of calf thymus DNA (.DELTA.Tm) showed that all the compds. have significant affinity for DNA. A comparison of .DELTA.Tms for the series with .DELTA.Tms of base-pair-specific DNA-binding compds., using homopolymers poly(dA).cntdot.poly(dT) and poly(dG-dC).cntdot.poly(dG-dC), indicated that the compds. show moderate specificity for AT base pairs. Lack of DNA helix extension, measured by viscometric titrn. with sonicated calf thymus DNA, indicated that the compds. do not bind to DNA by intercalation. Analogs of I with an odd no. of methylenes connecting the benzamidine rings had a higher affinity for DNA and homopolymers than analogs with an even no. of methylenes. All of the compds. contg. an amidino group meta to the linking chain showed lower polynucleotide affinity. These results suggest that the shape of the mols. was important for DNA binding. Mol. modeling studies showed a correlation between the DNA binding and the radius of curvature of mol. mechanics models of the mols. Monosubstitution on the benzamidine rings or replacement of the amidino group with the cyclic imidazolino group had no influence on the DNA-binding affinity of the compds. Substitution of NH for the ether oxygen connecting group of I had no effect on the DNA binding or base-pair specificity. Methylation of either of the nitrogen atoms of the imidazolino group to provide an analog of I with N-methylimidazolino groups decreased DNA affinity considerably. GC vs AT base-pair specificity as measured by .DELTA.Tm does not correlate with the radius of curvature. The exptl. and modeling results are consistent with DNA minor-groove binding.

ACCESSION NUMBER: 1992:75694 CAPLUS
DOCUMENT NUMBER: 116:75694
TITLE: Structure and DNA binding activity of analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine)
AUTHOR(S): Cory, Michael; Tidwell, Richard R.; Fairley, Terri A.
CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(3), 431-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7 125880-81-1 125880-82-2**
125880-83-3 125880-84-4 125880-85-5
125880-86-6 125880-87-7 125880-89-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-binding activity of)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

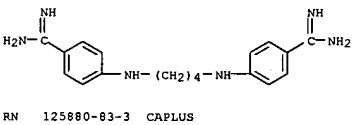
L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



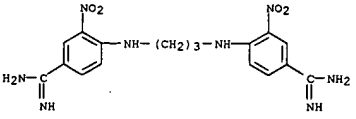
RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

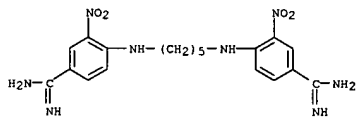


RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

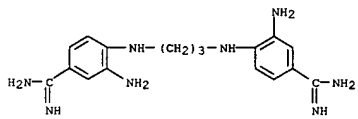


RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

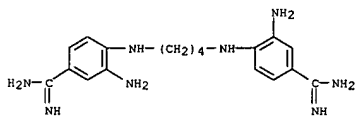
L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



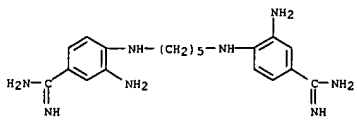
RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

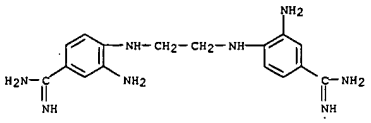


RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

L8 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



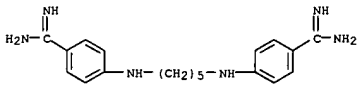
L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB 1,5-Di(4-amidinophenoxy)pentane (pentamidine) and 38 analogs of pentamidine were screened for in vitro against the enteric protozoan Giardia lamblia WB (ATCC 30957). All compds. were active against G. lamblia as measured by a [methyl-3H]thymidine incorporation assay. Antigiardial activity varied widely, with 50% inhibitory concns. (IC50s) ranging from 0.51 .+-. 0.13 .mu.M (mean .+-. std. deviation) for the most active compd. to over 100.0 .mu.M for the least active compds. The IC50 of the most potent antigiardial agent, 1,3-di(4-amidino-2-methoxyphenoxy)propane compared favorably with the IC50s of the compds. currently used to treat giardiasis, i.e., furazolidone (1.0 .+-. 0.03 .mu.M), metronidazole (2.1 .+-. 0.80 .mu.M), quinacrine HCl (0.03 .+-. 0.02 .mu.M), and tinidazole (0.78 .+-. 0.48 .mu.M). A mode of antigiardial activity for these compds. was suggested by the correlation obsd. between antigiardial activity and the binding of the compds. to calf thymus DNA and poly(dA).poly(dT).

ACCESSION NUMBER: 1991:554848 CAPLUS
DOCUMENT NUMBER: 115:154848
TITLE: Structure-activity relationships of pentamidine analogs against Giardia lamblia and correlation of antigiardial activity with DNA-binding affinity
AUTHOR(S): Bell, Constance A.; Cory, Michael; Fairley, Terri A.; Hall, James Edwin; Tidwell, Richard R.
CORPORATE SOURCE: Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1991), 35(6), 1099-107
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English

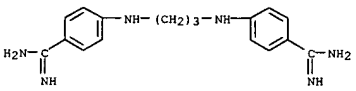
IT **124076-63-7 125880-81-1 125880-82-2 125880-83-3 125880-84-4 125880-86-6 125880-87-7 125880-89-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antigiardial activity of, structure in relation to)

RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

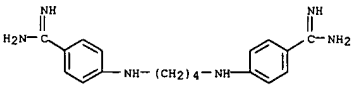


RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)

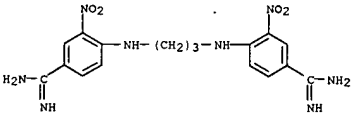
L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



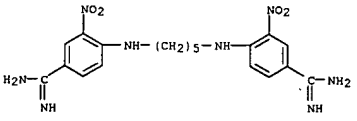
RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

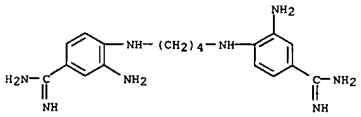


RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

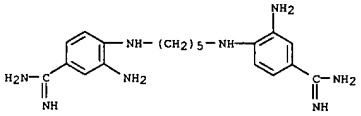


RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

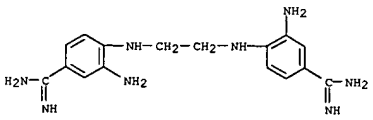
L8 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

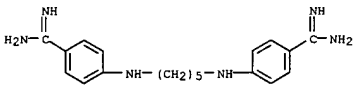


RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



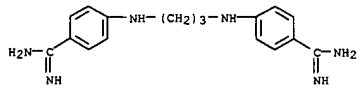
L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
AB The antiprotozoal compd. 1,5-di(4-amidinophenoxy)pentane (pentamidine) and
36 of its analogs were screened for in vitro activity against L. mexicana amazonensis clone 669 C4S (MHOM/BR/73M2269) and P. falciparum clones W2 (Indochina III/CDC) and D6 (Sierra Leone I/CDC). Pentamidine and each of the analogs tested exhibited activity in vitro against L. mexicana amazonensis and P. falciparum. The pentamidine analogs were more effective against he P. falciparum clones than against L. mexicana amazonensis. P. falciparum was extremely susceptible to these compds., with 50% inhibitory concns. as low as 0.03 .mu.M. While none of the analogs exhibited marked improvement in antileishmanial activity compared with pentamidine, 12 of the pentamidine analogs showed activity approx. equal to or greater than that of the parent compd. From the promising activity exhibited by the pentamidine analogs in this in vitro study and their potential for reduced toxicity relative to the parent drug, pentamidine-related compds. hold promise as new agents for the treatment of protozoal infections.

ACCESSION NUMBER: 1990:584205 CAPLUS
DOCUMENT NUMBER: 113:184205
TITLE: Structure-activity relationships of analogs of pentamidine against Plasmodium falciparum and Leishmania mexicana amazonensis
AUTHOR(S): Bell, Constance A.; Hall, James Edwin; Kyle, Dennis E.; Grogl, Max; Ohemeng, Kwasi A.; Allen, Margaret A.; Tidwell, Richard R.
CORPORATE SOURCE: Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1990), 34(7), 1381-6
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7 125880-81-1 125880-82-2 125880-83-3 125880-84-4 125880-86-6 125880-87-7 125880-89-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiprotozoal activity of, against Plasmodium falciparum and Leishmania mecicana amazonensis, structure in relation to)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

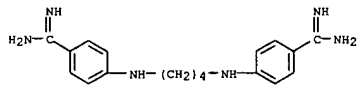


RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)

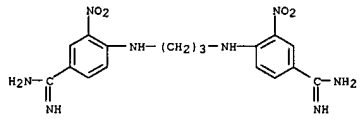
L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



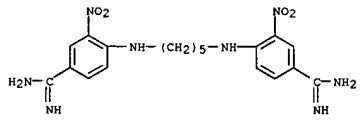
RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

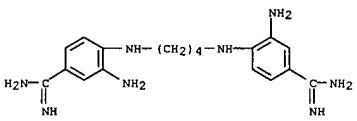


RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

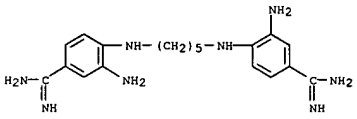


RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

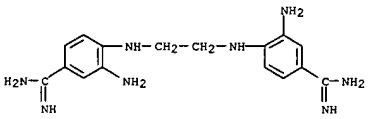
L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



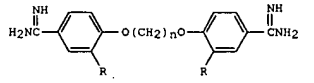
RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



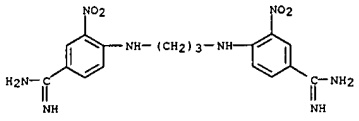
L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
GI



I, R=H, n=4
II, R=OMe, n=3

AB A series of 33 analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine) was synthesized for screening against a rat model of P. carinii pneumonia.
Twenty-five of the compds. showed efficacy against P. carinii pneumonia when compared to a saline-treated control group. Two compds., butamidine (I) and 1,3-bis(4-amidino-2-methoxyphenoxy)propane (II), were more effective than pentamidine in treating P. carinii pneumonia in the rat model of infection. In addn. to their activity against P. carinii pneumonia, the compds. were also evaluated for antitrypsin activity, ability to inhibit thymidylate synthetase, affinity for DNA, and toxicity.
No correlation was obsd. between the tested mol. interactions of the diamidines and their effectiveness against P. carinii pneumonia.

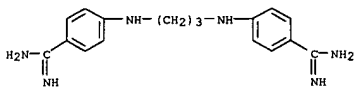
ACCESSION NUMBER: 1990:151252 CAPLUS
DOCUMENT NUMBER: 112:151252
TITLE: Analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine) in the treatment of experimental Pneumocystis carinii pneumonia
AUTHOR(S): Tidwell, Richard R.; Jones, Susan Kilgore; Geratz, J. Dieter; Ohemeng, Kwasi A.; Cory, Michael; Hall, James Edwin
CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Journal of Medicinal Chemistry (1990), 33(4), 1252-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:151252
IT **125880-66-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenation of)
RN 125880-66-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

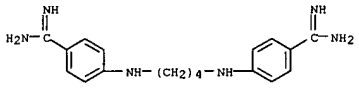
IT **109563-82-8P 125880-64-0P 125880-65-1P**
125880-67-3P 125880-68-4P 125880-69-5P
125880-70-8P 125880-73-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Pneumocystis carinii pneumonia inhibition by and toxicity of)

RN 109563-82-8 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)



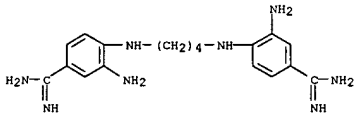
●2 HCl

RN 125880-64-0 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)



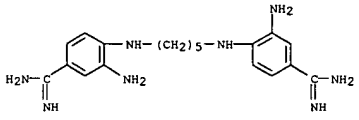
●2 HCl

RN 125880-65-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)



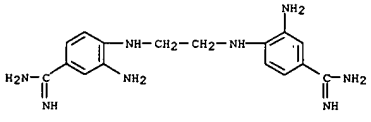
●4 HCl

RN 125880-70-8 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

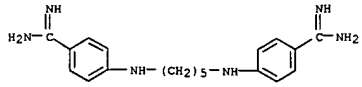
RN 125880-73-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

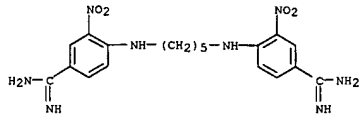
IT **124076-63-7 125880-81-1 125880-82-2**
125880-83-3 125880-84-4 125880-85-5
125880-86-6 125880-87-7 125880-89-9
RL: BIOL (Biological study)
(Pneumocystis carinii pneumonia inhibition by and toxicity of)

RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX



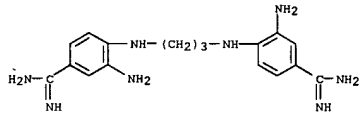
●2 HCl

RN 125880-67-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

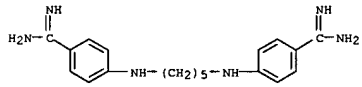
RN 125880-68-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)



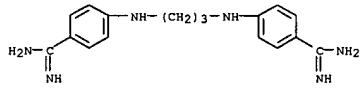
●4 HCl

RN 125880-69-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)

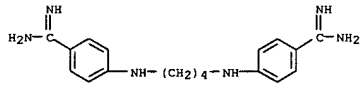
NAME)



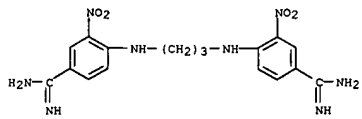
RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)

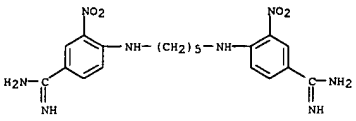


RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

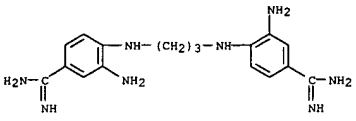


RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)

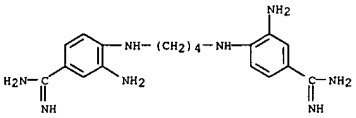
L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



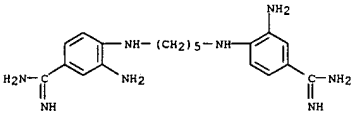
RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

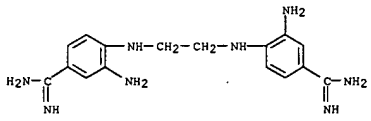


RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

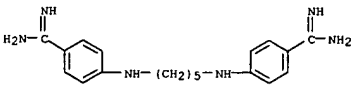
L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



L8 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB A HPLC method was developed for the detection and quantification of pentamidine and pentamidine analogs of chemotherapeutic value in order to measure their concn. in physiol. fluids. The compds. were extd. from urine over octadecyl solid-phase extn. columns, followed by chromatog. sepn. with an octadecyl reversed-phase column. For the mobile phase, a gradient of 31.5-37.5% MeCN in water, with Na heptanesulfonate and N(Me)4Cl as ion modifiers, was used. This method was used to reliably detect levels as low as 341 ng/mL without concn. of the compds. during the solid-phase extn. The assay was used to det. the effectiveness of several solid-phase extn. columns for isolating the compds. of interest and to quantify the amt. of pentamidine and its analogs contained in the urine of dosed rats.

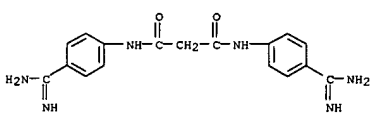
ACCESSION NUMBER: 1990:87 CAPLUS
DOCUMENT NUMBER: 112:87
TITLE: High-performance liquid chromatographic method for the quantification of several diamidine compounds with potential chemotherapeutic value
AUTHOR(S): Berger, Bradley J.; Hall, James Edwin; Tidwell, Richard R.
CORPORATE SOURCE: Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Journal of Chromatography (1989), 494, 191-200
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **124076-63-7**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in urine by HPLC)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB Similarities and differences of trypsin (I) and plasma kallikrein (II) are interpreted. Various amidines were tested for inhibition of II activity with N-.alpha.-tosyl-L-arginine Me ester (TAME) as substrate. Results with 150 amidines in vitro showed that aliphatic amidines were inactive. Some aromatic amidines, bis-amidines more than mono-amidines, had considerable inhibitory action. All amidines acted as competitive inhibitors. Substitution of the amidine group gave a loss of activity. Results are tabulated with structural formulas of 7 aromatic amidines inhibiting kallikrein for TAME substrate, and for 6 aromatic amidines inhibiting TAME hydrolysis by kallikrein, I, thrombin, and plasmin. Several amidines were tested against burns in guinea pigs and turpentine-induced edema in the pleural cavity of rats. The results varied with exptl. conditions, but some amidines had activity against the exptl. irritations. In general, the in vitro inhibitory activity of amidines was more specific than in vivo activity. Compd. I.C.I. 54,394, had marked activity against kallikrein, trypsin, thrombin, and plasmin in vitro.

ACCESSION NUMBER: 1971:120730 CAPLUS
DOCUMENT NUMBER: 74:120730
TITLE: Inhibition of guinea pig plasma kallikrein by amidines
AUTHOR(S): Davies, George Edward; Lowe, J. S.
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind., Macclesfield/Cheshire, UK
SOURCE: Advances in Experimental Medicine and Biology (1970), 8, 453-60
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **32152-41-3**
RL: BIOL (Biological study)
(kallikreins inhibition by)
RN 32152-41-3 CAPLUS
CN Propanediamide, N,N'-bis[4-(aminoiminomethyl)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
GI For diagram(s), see printed CA Issue.
AB cf. CA 55, 8344c. A series of 4,4'-diamidinodiphenylamines with substituents in the C6H6 rings and (or) on the central amino group was described. Most of the compds. were active against Trypanosoma rhodesiense, but the activity was less against T. congolense. The most active compd. was 4,4'-diamidino-2-methoxydiphenylamine-2HCl, with a therapeutic ratio of 7.5 against the latter organism. Treatment of 4-amino-3-methylbenzonitrile in C5H5N with BzCl gave 75% N-benzoyl-4-cyano-2-methylaniline, m. 153.degree. (alc.). N-Benzoyl-4-cyano-2-nitroaniline similarly obtained m. 144-6.degree.. A mixt. of N-benzoyl-p-cyanoaniline (1 mole), 0.98 mole PCl5, and 4 moles CCl4 was refluxed and the solvent and POCl3 removed in vacuo. The residual imidoyl chlorides, readily hydrolyzed by moisture, were not further purified but condensed directly with various p-hydroxybenzonitriles by one of the following processes. (A) p-Hydroxybenzonitrile (1.1 moles) was added to 1 mole NaOEt in alc., 1 mole benzimidoyl chloride (Ia) in Et2O-CHCl3 added, then 0.25 mole anhyd. Na2CO3, the mixt. stirred 1-2 hrs. at 0.degree., then 3-4 hrs. at room temp., left overnight, the solid collected, and recrystd. from alc. (B) The Na salt of 1 mole p-hydroxybenzonitrile in dry C5H5N was mixed with molten Ia, heated a few min. on the steam bath, H2O added, and the oily ppt. crystd. and recrystd. (C) The p-hydroxybenzonitrile (1 mole) and Ia were melted together, 1.5 moles anhyd. NEt3 added, the mixt. refluxed 2 hrs., H2O and a slight excess AcOH added; the benzimidates generally sepd. as oils which soon crystd. The following HC:CH.C(CN):CH.CR:CN:CPhOC:CR1.C H:C(CN).CH:CR2 (I) were thus obtained (R, R1, R2, process, % yield, and m.p. given): H, Me, H, A, 63, 142.5.degree.; H, Me, H, B, 39, 136-8.degree.; H, Me, H, C, 76, 140-1.degree.; Me, H, H, A, 45, 104.5.degree.; Me, H, H, B, -, 102-4.degree.; Me, Me, H, A, 79, 125-9.degree.; Me, Me, H, B, 58, 123-6.degree.; Me, Me, H, C, 83, 125-7.degree.; H, Cl, H, A, 25, 135-6.degree.; Me, Cl, H, A, 36, 124.degree.; H, Cl, Cl, A, 24, 167-8.degree.; H, NO2, H, A, 47, 136.degree.; H, NO2, H, B, 69, 135-6.degree.; H, NO2, H, C, 64, 134-6.degree.; NO2, H, H, A, 78, 192.degree.; NO2, NO2, H, B, 96, 198.degree.; H, OMe, H, C, 60, 147-8.degree.. The rearrangement of I to benzoyldiphenylamines (II) was carried out as follows except in 3 cases of I (R = R2 = H, R = NO2; R = NO2, R1 = R2 = H; and R = R1 = NO2, R2 = H) I were dissolved in an equal wt. of Dowtherm and the soln. refluxed 1-2 hrs. II were isolated by addn. of Et2O and crystd. from alc. II (R1 = R2 = H, R = Me) was not characterized but was hydrolyzed directly to the corresponding diphenylamine. I (R = R2 = H, R1 = NO2) rearranged smoothly in refluxing anisole and even in refluxing C5H5N, tars being formed at higher temps. Two I (R = NO2, R1 = R2 = H; R = R1 = NO2, R2 = H) were unaffected at the lower temps. and decompd. at 200.degree.. The following II, HC:CH.C(CN):CH.CR:CNBzC:CR1.CH:C(CN).CH:CR2, were thus obtained (R, R1, R2, % yield, and m.p. given): H, Me, H, 94, 165-7.degree.; Me, Me, H, 98, 159-60.degree.; H, Cl, H, 84, 170-2.degree.; Me, Cl, H, 80, 167-8.degree.; H, Cl, Cl, 54, 204-5.degree.; H, NO2, H, 99, 234-7.degree.; H, OMe, H, 88, 152-4.degree.. CR:CH.C(CN):CH.CH:CNHCH:CH.CH:C(CN).CH:CR1 (III) were next. prepd. Compds. nos. 1-5 (see further) were prepd. by hydrolysis of the corresponding II. A 10% NaOH soln. in 75% (CH2OH)2 was added in 1 portion to the II compd. in 3-4 parts refluxing ethylene

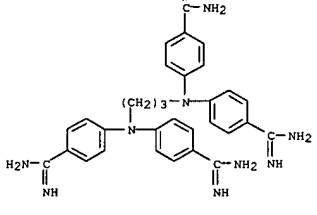
L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
glycol, the mixt. refluxed a few min., and the product pptd. by H2O and recrystd. (AcOH). Compd. no. 6A was prepd. by hydrolysis of the corresponding II with K2CO3 in ethylene glycol-anisole contg. a little H2O. The product resisted purification but an almost theoretical yield of pure nitro compd. (no. 6B) was obtained as follows. 4,4'-Dicyanodiphenylamine (40 g.) was ground with 200 ml. AcOH, 400 ml. concd. HNO3 added, and after 25 min. H2O added to yield compd. no. 6B, crystd. from anisole; no. 7 (83%) was obtained by addn. of 45 g. reduced Fe to 24 g. 4,4'-dicyano-2-nitrodiphenylamine in 60 ml. refluxing HCONMe2 and 40 ml. AcOH, adding after 0.5 hr. 400 ml. hot H2O, filtering the mixt. and working up sep. the ppt. and the filtrate. Compds. nos. 12-15 were prepd. by demethylation of 4,4'-dicyano-2-methoxydiphenylamine to give the OH deriv. At the required temp. (197-203.degree.), part of the mixt. tended to sublime, a little Dowtherm was added, after 4 hrs. the mixt. stirred with dil. alc., and the solid dissolved in HCONMe2-dioxane. Any MeO compd. was pptd. by excess 5N NaOH; acidification gave the 2-OH deriv. The other 2-alkoxy derivs. were obtained by alkylation of this with the appropriate halide and K2CO3 in refluxing Me2CO. The following III were thus obtained (no., R, R1, % yield, and m.p. given): (1), Me, H, 85, 222.degree.; (2), Cl, H, 60, 211.degree.; (3), Me, Me, 38, 199-200.degree.; (4), Me, Cl, 73, 198.degree.; (5), OMe, H, 86, 145-6.degree.; (6A), NO2, H, -, 186-91.degree.; (6B), NO2, H, 95, 191.degree.; (7), NH2, H, 83, 238-9.degree.; (8), NHAc, H, 75, 238-40.degree.; (9), HNBz, H, -, 233-5.degree.; (10), Cl, Cl, -, 243-4.degree.; (11), OH, H, 55, 257-8.degree.; (12), OEt, H, 76, 169-70.degree.; (13), OPr, H, 73, 135-6.degree.; (14), OCH2CH:CH2, H, 70, 135-6.degree.; (15), Bu, H, 80, 114-15.degree.. 1,3-Trimethylene bis(p-toluenesulfonate) (86%), m. 95-6.degree., 1,5-pentamethylene bis(p-toluenesulfonate) (85%), m. 80.degree. (alc.), and 2-hydroxyethyl p-toluenesulfonate, a sirup (phenylurethan m. 135-6.degree.), were prepd. by the Ag salt method. N-Alkyl derivs. were prepd. by treating 1 mole 4,4'-dicyanodiphenylamine with 1.2-1.5 moles requisite alkyl p-toluenesulfonate, 1 mole K2CO3, anisole, and a trace of Cu bronze under reflux, the H2O removed, and replaced by anisole, after refluxing 3-4 hrs. the solvent added, the mixt. filtered, the solvent removed, and the residue recrystd. from alc. N-Aryl-4,4'-dicyanodiphenylamines were prepd. by treatment of 1 mole 4,4'-dicyanodiphenylamine in the presence of K2CO3 and a trace of Cu bronze in refluxing PhNO2 4-6 hrs. with an excess of (a) PhI, (b) p-bromonitrobenzene, or (c) p-bromobenzonitrile. The products from (a) or (b) were isolated by addn. of CHCl3 and evapn. The solid from (c) was collected, washed, and the dried solid extd. with hot HCONMe2. 4,4'-Dicyano-N-(p-nitrophenyl)-diphenylamine (1.7 g.) in 15 ml. refluxing HCONMe2 and 2.5 ml. AcOH treated with reduced Fe gave 1.25 g. amine. The following N-substituted 4,4'-dicyanodiphenylamines were thus obtained (N-substituent, solvent for crystn., % yield, and m.p. given): Me, alc., 89, 153.degree.; Et, alc., 55, 122-3.degree.; Pr, alc., 63, 96.degree.; allyl, alc., 71, 111-12.degree.; Bu, Et2O, 41, 80-1.degree.; C6H13, alc., 60, 77.degree.; (CH2)3, dioxane, 50, 211-12.degree.; Ph, alc., 78, 190-1.degree.; p-O2NC6H4, PhNO2, 80, 346.degree.; p-H2NC6H4, -, 73, 275.degree.; p-NCC6H4, HCONMe2, 57, 342.degree.. 4,4'-Dicyano-2-methoxydiphenylamine (1 g.), 1 g. p-MeC6H4SO3Me, 0.8 g. K2CO3, a trace of Cu bronze, and 10 ml. anisole refluxed 3 hrs. gave 0.95 g. 4,4'-dicyano-2-methoxy-N-methyldiphenylamine, m. 149-50.degree. (alc.). 4,4'-Dicyano-2-methyldiphenylamine and p-MeC6H4SO3Me gave 94%

L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
4,4'-dicyano-2,N-dimethyldiphenylamine, m. 112.degree. (alc.). Refluxing 5 g. 2-amino-4,4'-dicyanodiphenylamine in 25 ml. 98-100% HCO2H 1.5 hrs. gave 5-cyano-1-(p-cyanophenyl)benzimidazole, m. 289.degree. (AcOH). 2-Amino-4,4'-dicyanodiphenylamine (12.5 g.), 50 ml. C5H5N, and 30 ml. Ac2O refluxed 0.5 hr. gave 12 g. 2-acetamido deriv., m. 238-40.degree. (decompn.), converted by refluxing 1.5-2.0 hrs. in 40 ml. Dowtherm into 8.4 g. 5-cyano-1-(p-cyanophenyl)-2-methylbenzimidazole, m. 233.degree.. 5-Cyano-1-(p-cyanophenyl)-2-phenylbenzimidazole similarly prepd., m. 182.degree., solidified, and m. 199.degree.. 2-Amino-4,4'-dicyanodiphenylamine (10 g.), 100 ml. alc., 5 ml. 7.5N isethionic acid, 10 ml. H2O, and 5 ml. concd. HCl treated at 10.degree. with 5 g. NaNO2 in 10 ml. H2O and 5 ml. alc. and kept 3 hrs. at room temp. gave 95% 5-cyano-1-(p-cyanophenyl)benzo-1,2,3-triazole, m. 284.degree. (dioxane). 4,4'-Dicyano-2-nitrodiphenylamine (1 g.), 2 ml. ClCO2Et, 1 g. K2CO3, and 10 ml. Me2CO refluxed 2 hrs. gave 0.8 g. 4,4'-dicyano-N-ethoxycarbonyl-2-nitrophenylamine, yellow crystals, m. 123-4.degree. (alc.). Similarly, 4,4'-dicyano-2-hydroxydiphenylamine gave 4,4'-dicyano-N-ethoxycarbonyl-2-ethoxycarbonyloxydiphenylamine, m. 131.5-2.5.degree. (alc.). If the reaction was carried out with an excess of dinitrile, the product was 6-cyano-3-(p-cyanophenyl)benzoxazolone (IV), m. 290.degree.. IV was best prepd. by the following procedure. NaOH (1.46 g.) in a little H2O and sufficient alc. to make 24 ml. added to 13.8 g. of the diethoxycarbonyl compd. in 50 ml. dioxane and 50 ml. alc., left 2-3 hrs., concd. HCl added, and the whole dild. with H2O gave 8.8 g. IV. The nitriles were converted into the amidines (V), through the imidates, by the usual Pinner procedure. V were often isolated as HCl salts. Some of the more sol. salts were not too easily crystd. In such cases the bases were isolated and converted into the acetates. The following diamidines, HC:CH.[H2NC(:NH)]C:CH.CR:CNR1C:CR2.CH:C[C-(:NH)NH2].CH:CH, were thus prepd. (R, R1, R2, solvent, time in days, amidine salt, crystn. solvent, % yield, and m.p. given): Me, H, H, CHCl3, 4, 2HCl, H2O, 94, -; H, Me, H, CHCl3, 2, 2HCl, aq. alc. and Et2O, 63, 330.degree.; H, Et, H, alc., 1, 2HCl, aq. alc.-Et2O, 57, above 300.degree.; Cl, H, H, CHCl3, 3, 2HCl, H2O, 38, above 300.degree.; H, Ph, H, CHCl3-dioxane, 6, 2HCl, aq. Me2CO, 70, above 300.degree.; H, Bz, H, CHCl3, 12, 2HCl, aq. Me2CO, 31, 280.degree.; Me, Me, H, CHCl3, 7, 2HCl, aq. Me2CO-alc., 47, 285.degree.; H, Bu, H, CHCl3, 4, diacetate, aq. Me2CO, 63, 275-80.degree.; H, allyl, H, CHCl3, 5, diacetate, H2O or aq. Me2CO, 67, 271-3.degree.; H, Pr, H, CHCl3-Et2O, 1, 2HCl, aq. Me2CO, 78, 232-8.degree.; H, p-C6H4C(:NH)NH2, H, CHCl3-dioxane, 10, 3HCI, aq. Me2CO, 50, 370-5.degree.; NH2, H, H, alc., 6, 2HCl, H2O, 54, 310.degree.; H, (CH2)3, H, alc., 2, 4HCl, aq. Me2CO, 67, 300-10.degree.; H, p-C6H4NH2, H, alc., 6, diacetate, aq. Me2CO, 37, 169.degree.; Me, Bz, Cl, alc., 1, diacetate, AcOH, -, 225-30.degree.; Me, H, Cl, dioxane, 2, 2HCl, H2O, 70, above 350.degree.; H, C6H13, H, CHCl3-Et2O, 6, diacetate, aq. Me2CO, 63, 265.degree.; Cl, H, Cl, CHCl3-Et2O, 4, 2HCl, 40% alc., 90, above 350.degree.; Me, H, Me, dioxane, 5, 2HCl, aq. Me2CO, 75, above 350.degree.; OMe, H, H, CHCl3, 3, 2HCl, aq. Me2CO, 64, 110-15.degree.; OH, H, H, dioxane-Et2O, 4, 2HCl, aq. Me2CO, 54, 338-40.degree.; OEt, H, H, CHCl3, 6, 2HCl, aq. Me2CO, 85, 115-17.degree.; OBu, H, H, CHCl3, 1, 2HCl, aq. Me2CO, 85, 133-4.degree.; OCH:CHMe, H, H, CHCl3, 3, 2HCl, aq. Me2CO, 79, 108-10.degree.; OPr, H, H, CHCl3, 2, 2HCl, aq. Me2CO, 78, 125-8.degree.; H, NO, H, CHCl3, -, 2HCl, aq. Me2CO, 88, greater than 300.degree.; OMe, Me, H, CHCl3, 2, dipropionate, aq. Me2CO,

L8 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
44, 193-201.degree.; OMe, NO, H, CHCl3, -, diacetate, aq. Me2CO, 69, 192-3.degree.; Me, NO, H, CHCl3, -, diacetate, aq. Me2CO, 93, 227-8.degree.. Addn. of 5.5 g. NaNO3 in 15 ml. H2O to a cold soln. of 4,4'-diamidino-2-methoxydiphenylamine 2HCl in H2O pptd. the sparingly sol. nitrite as a solid. 2N HCl (40 ml.) added during 5-10 min. and the ppt. redissolved, the soln. kept 1 hr., 25 ml. 5N NaOH added, the nitrosoamine base collected and treated with AcOH gave 8 g. of the diacetate. The diimidoate was prepd. in CHCl3-dioxane and 76% 5-amidino-1-(p-amidinophenyl)benzimidazole-2HCl collected, m. 305.degree. (aq. Me2CO). 5-Amidino-1-(p-amidinophenyl)-2-methylbenzimidazole-2HCl (67%) (H2O) and 5-amidino-1-(p-amidinophenyl)benzo-1,2,3-triazole-2HCl (78%) (Me2CO-dil. HCl) were prepd. similarly.

ACCESSION NUMBER: 1961:87461 CAPLUS
DOCUMENT NUMBER: 55:87461
ORIGINAL REFERENCE NO.: 55:16523h-i,16524a-i,16525a-i,16526a-d
TITLE: Search for chemotherapeutic amidines. XVIII. Substituted 4,4'-diamidinodiphenylamines
AUTHOR(S): Easson, A. P. T.
CORPORATE SOURCE: May & Baker Ltd., Dagenham, UK
SOURCE: J. Chem. Soc. (1961) 1029-37
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

IT **108651-36-1**, Benzamidine, 4,4',4'',4'''-(trimethylenedinitrilo)tetra-, tetrahydrochloride (prepn. of)
RN 108651-36-1 CAPLUS
CN Benzamidine, 4,4',4'',4'''-(trimethylenedinitrilo)tetra-, tetrahydrochloride (6CI) (CA INDEX NAME)



●4 HCl

L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB cf. CA 55, 5521e. The title compds. and the piperazine deriv., 1,4-bis(p-amidinophenyl)piperazine (I) were described. They had no significant trypanocidal activity. p-Aminobenzamidine-HCl (8.5 g.) in 50 ml. alc. and 2 ml. 40% HCHO refluxed 0.5 hr. gave 4.3 g. bis(p-amidinoanilino)methane-2HCl, m. 236-8.degree. (MeOH-Me2CO). CuCN (6.8 g.) and 10 ml. C5H5N heated to 120-30.degree., 9.25 g. 1,2-bis(p-bromoanilino)ethane added, the temp. raised to 215-20.degree., the C5H5N distd., the melt stirred at 195-200.degree. 3 hrs., added to 20 g. KCN in 50 ml. H2O (the oil sepd. and hardened), the liquor poured off, the mass ground with 2N HCl to give 14.5 g. solid, this sublimed, and the yellow sublimate (300-10.degree./0.1 mm.) (0.45 g.) crystd. gave 0.33 g. 1,2-bis(p-cyanoanilino)ethane (II), m. 205-6.degree. (AcOH). p-Aminobenzonitrile (100 g.), 142 g. NaHCO3, 160 g. C2H4Br2, and 400 ml. EtOCH2CH2OH refluxed 18 hrs., the mixt. cooled to 10.degree., the insol. material removed, the filtrate dild. with H2O, and the brown granular solid collected. p-Aminobenzonitrile (51 g.) was recovered from the mother liquors. The brown solid crystd. gave 18 g. product, sublimed to afford 9 g. II. The 1st filtered product afforded 6.6 g. 1,4-bis(p-cyanophenyl)piperazine (III), yellow needles, m. 275-7.degree. (anisole). p-Aminobenzonitrile (5 g.), 4.25 g. anhyd. Na2CO3, and 7.1 g. C2H4Br2 refluxed 3 hrs. at 150-5.degree., cooled, filtered, and the solid crystd. gave 1.4 g. III. II (27.5 g.) in 650 ml. EtOCH2CH2OH at 0-5.degree. satd. with HCl, left 10 days and the mixt. treated with 390 ml. satd. alc. NH3 at 55-60.degree. gave 7.5 g. 1,2-bis(p-aminoanilino)ethane-2HCl (IV), plates, m. 353.degree. (decompn.) IV (7.5 g.) in 800 ml. H2O treated at 10-15.degree. with 50% NaOH gave 6.4 g. product, which suspended in 80 ml. MeOH with methanesulfonic acid gave 7.1 g. 1,2-bis(p-amidinoanilino)ethane di(methanesulfonate), m. 301-2.degree. (MeOH). III (8.4 g.) in 150 ml. EtOCH2CH2OH satd. at 0.5.degree. with HCl gave I.2HCl. I.2HCl (6 g.) in 750 ml. H2O basified and the base treated with 20 ml. 2N isethionic acid gave 5.5 g. I diisethionate, yellow needles, m. 328.degree. (decompn.) (MeOH). p-Aminobenzonitrile (12 g.) in 100 ml. 2N HCl and 150 ml. H2O stirred 1 hr. with 12 ml. 1,1,3,3-tetraethoxypropane, the 15 g. solid washed, and a soln. in 300 ml. 96% aq. C5H5N treated with 300 ml. H2O gave 11 g. 1-(p-cyanoanilino)-3-(p-cyanophenylimino)-1-propene, m. 227-9.degree.. p-Aminobenzonitrile (11.8 g.), 5.2 ml. 1,3-dibromopropane, 8.4 g. NaHCO3, and 50 ml. EtOCH2CH2OH refluxed overnight gave 3 g. 1,3-bis(p-cyanoanilino)propane (V), m. 159-61.degree. (aq. alc.). 1-(p-Cyanoanilino)-3-(p-cyanophenylimino)-1-propene (11 g.) in 700 ml. HCONMe2 hydrogenated at room temp. with 1.6 g. PtO2 1.5 hrs. gave 4.15 g. V. 1,3-Bis(p-cyanoanilino)propane (10 g.) in 200 ml. alc. satd. with HCl at 0-5.degree. and the diimidoester-2HCl which sepd. during 1 week (14.1 g.) dissolved in 100 ml. refluxing H2O and 30 ml. satd. NaCl gave 5.8 g. 1,3-bis(p-amidoanilino)propane-2HCl, yellow plates, m. 316-18.degree. (decompn.). Na glutaconic aldehyde-2H2O (1.55 g.) in 50 ml. H2O added at 80-90.degree. to 2.36 g. p-aminobenzonitrile in 20 ml. 2N H2SO4 and 120 ml. H2O, the mixt. stirred a further 10 min., and filtered gave 2.5 g. 1-(p-cyanoanilino)-5-(p-cyanophenylimino)-1,3-pentadiene, m. 140-4.degree. (decompn.), which (2.4 g.) in 100 ml. HCONMe2 reduced at 30-5.degree. over 0.24 g. PtO2, the ppt. filtered off, washed, and extd. with CHCl3 gave 1.8 g. brown solid, m. 160-70.degree.. Attempts

L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

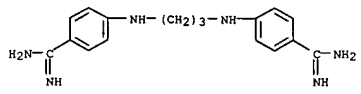
to purify this product were unsuccessful. The aq. dimethylformamide filtrate gave 0.2 g. p-aminobenzonitrile. p-Aminobenzonitrile (94.4 g.), 97.6 g. hexamethylene dibromide, 67.2 g. NaHCO3, 400 ml. EtOCH2CH2OH, and a crystal of iodine refluxed 24 hrs., the solvent evapd., the residual oil cooled, stirred with 2 l. 2N HCl, extd. with CHCl3, and the solvent removed gave 16 g. 1,6-bis(p-cyanoanilino)hexane (VI), prismatic needles, m. 165-7.degree. (AcOH). Similarly, 15 g. VI in 180 ml. EtOCH2CH2OH satd. at 0-5.degree. with HCl gave the di-HCl salt, converted to 5.2 g. 1,6-bis(p-amidinoanilino)hexane diisethionate, prisms, m. 238-40.degree. (H2O and MeOH).

ACCESSION NUMBER: 1961:43097 CAPLUS
DOCUMENT NUMBER: 55:43097
ORIGINAL REFERENCE NO.: 55:8344c-i,8345a-b
TITLE: Search for chemotherapeutic amidines. XVII. .alpha.,.omega.-Bis(p-amidinoanilino)alkanes
AUTHOR(S): Berg, S. S.
CORPORATE SOURCE: Northern Polytechnic, London
SOURCE: J. Chem. Soc. (1960) 5172-6
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

IT **109563-82-8**, Benzamidine, 4,4'-(trimethylenediimino)di-, dihydrochloride
(prepn. of)

RN 109563-82-8 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis-, dihydrochloride
(9CI) (CA INDEX NAME)



●2 HCl

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FULL ESTIMATED COST                                        88.69     416.12

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PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L9      STRUCTURE UPLOADED

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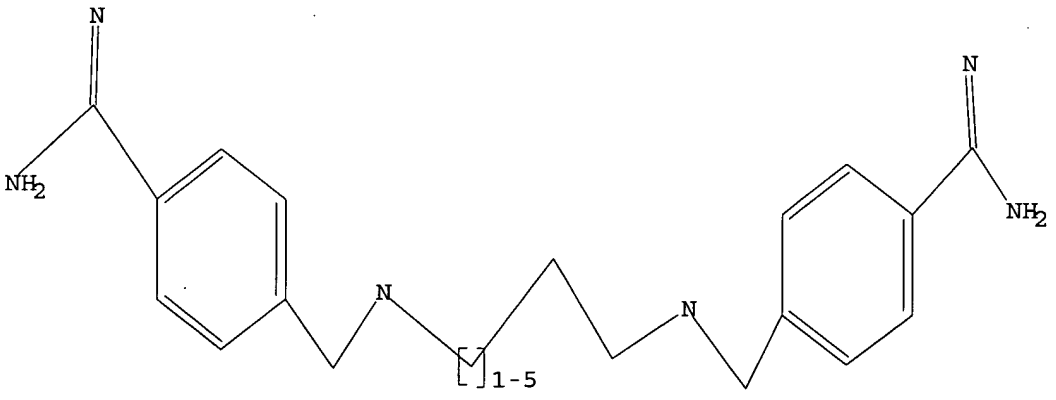

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SAMPLE SCREEN SEARCH COMPLETED -     17 TO ITERATE

100.0% PROCESSED      17 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           93 TO      587
PROJECTED ANSWERS:               0 TO        0

L10           0 SEA SSS SAM L9

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FULL SEARCH INITIATED 16:29:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    433 TO ITERATE

100.0% PROCESSED     433 ITERATIONS                               3 ANSWERS
SEARCH TIME: 00.00.01

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
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FILE COVERS 1907 - 6 Feb 2003  VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003  (20030205/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s l11
L12           5 L11

=> d l12 1-5 abs ibib hitstr
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L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Polyamine or polyamine analog-amino acid conjugates (M)-N(E)-(B-A-B-NH)4-E or (M)-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [M is an amino acid; A is a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B is a bond, alkyl, or alkenyl; E is H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl], including salts or stereoisomers, were prepd. for use as antiviral agents. An example is the polyamine glutamine conjugate SL-11165 [NH2CH(CH2CH2CONH2)CON(Et)(CH2CH2CH2CH2NH)4Et.bul.5HCl]. Thus, (E)-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NHEt was prepd. by a multi-step sequence starting from 4-bromobutanenitrile, N-(mesitylsulfonyl)ethanamine, and (E)-2-butene-1,4-diol.

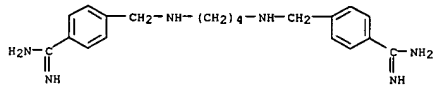
ACCESSION NUMBER: 2002:888472 CAPLUS
DOCUMENT NUMBER: 137:384565
TITLE: Preparation of polyamine or polyamine analog-amino acid conjugates as antiviral agents
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.; Gutierrez, Jesus A.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA; Eli Lilly & Company
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002091989	A2	20021121	WO 2001-US43887	20011108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

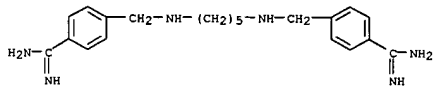
PRIORITY APPLN. INFO.: US 2000-246804P P 20001108
OTHER SOURCE(S): MARPAT 137:384565
IT **304911-05-5P**, SL 11137 **304911-11-3P**, SL 11134
304911-12-4P, SL 11136
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)
RN 304911-05-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



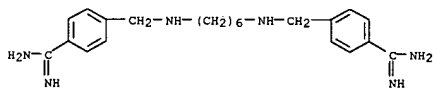
●4 HCl

RN 304911-11-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

RN 304911-12-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Conjugates of polyamines analogs conjugated to at least one amino acid of formula M-N(E)-(B-A-B-NH)4-E or M-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [wherein M = independently an amino acid, esp. glutamine, asparagine, lysine, ornithine, arginine, histidine, or citrulline; A = independently a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B = independently a bond, alkyl, or alkenyl; E = independently H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; and salts or stereoisomers thereof] were tested and claimed for pharmaceutical use as anticancer agents. For example, the polyamine glutamine conjugate SL-11165 [NH2CH(CH2CH2CONH2)CON(Et)(CH2CH2CH2CH2NH)4Et.bul.5HCl] exhibited ID50 values of >31.65, 4.1, and >31.25 against the DuPro, PC-3, and LnCap prostate cancer cell lines, resp. In addn., conformationally restricted polyamine analogs were prepd. Thus, (E)-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NH Et was prepd. in a multi-step sequence starting from 4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol.

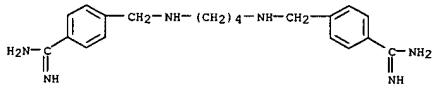
ACCESSION NUMBER: 2002:368258 CAPLUS
DOCUMENT NUMBER: 136:386292
TITLE: Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as anticancer agents
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038105	A2	20020516	WO 2001-US43585	20011108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

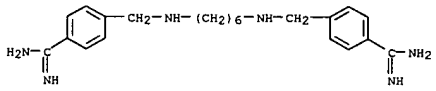
AU 2002035126 A5 20020521 AU 2002-35126 20011108
PRIORITY APPLN. INFO.: US 2000-246804P P 20001108
WO 2001-US43585 W 20011108
OTHER SOURCE(S): MARPAT 136:386292
IT **304911-05-5P**, SL 11137 **304911-12-4P**, SL 11136
RL: SPN (Synthetic preparation); PREP (Preparation)
(polyamine; prepn. of conformationally restricted polyamines and use of polyamine amino acid conjugates as anticancer agents)
RN 304911-05-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



●4 HCl

RN 304911-12-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

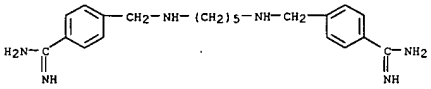
L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Microsporidia are eukaryotic obligate intracellular protists that are emerging pathogens in immunocompromised hosts, such as patients with AIDS or patients who have undergone organ transplantation. We have demonstrated in vitro and in vivo that synthetic polyamine analogs are effective antimicrosporidial agents with a broad therapeutic window. CD8-knockout mice or nude mice infected with the microsporidian Encephalitozoon cuniculi were cured when they were treated with four different novel polyamine analogs at doses ranging from 1.25 to 5 mg/kg of body wt./day for a total of 10 days. Cured animals demonstrated no evidence of parasitemia by either PCR or histol. staining of tissues 30 days after untreated control animals died.

ACCESSION NUMBER: 2002:30291 CAPLUS
DOCUMENT NUMBER: 136:318859
TITLE: Novel synthetic polyamines are effective in the treatment of experimental microsporidiosis, an opportunistic AIDS-associated infection
AUTHOR(S): Bacchi, Cyrus J.; Weiss, Louis M.; Lane, Schenella; Frydman, Benjamin; Valasinas, Aldonia; Reddy, Venodhar; Sun, Jerry S.; Marton, Laurence J.; Khan, Imitiaz A.; Moretto, Magali; Yarlett, Nigel; Wittner, Murray
CORPORATE SOURCE: Haskins Laboratories and Departments of Biology and Chemistry, Pace University, New York, NY, 10038-1598, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(1), 55-61
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **304911-11-3**, SL 11134
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11134; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-11-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



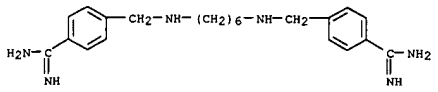
●4 HCl

IT **304911-12-4**, SL 11136
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11136; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-12-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-,

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)

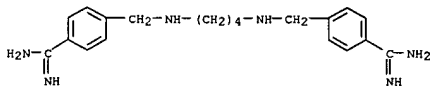
tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

IT **304911-05-5**, SL 11137
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11137; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-05-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Novel conformationally restricted polyamines, such as E-NH-(B-A-B-NH)4-E [A, E = bond, alkyl, alkenyl, alkynyl, cycloalkyl, cycloaryl, cycloalkenyl; B = bond, alkyl, alkenyl], were prepd. for pharmaceutical use as anticancer agents. Thus, (E)-EtNH(CH2)4NHCH2CH:CHCH2NH(CH2)4NHEt was prepd. in a multistep sequence starting from mesityl chloride 4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol. The prepd. polyamines were tested for antiproliferative activity against human prostate cancer cell lines, such as PC3 and DUPRO.

ACCESSION NUMBER: 2000:790505 CAPLUS
DOCUMENT NUMBER: 133:350095
TITLE: Preparation of conformationally restricted polyamine analogs as disease therapies
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Reddy, Venodhar K.; Valasinas, Aldonia; Blokhin, Andrei V.; Basu, Hirak S.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066587	A2	20001109	WO 2000-US11591	20000427
WO 2000066587	A3	20010125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1177197	A2	20020206	EP 2000-928583	20000427
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BR 2000010701	A	20020213	BR 2000-10701	20000427
JP 2002543202	T2	20021217	JP 2000-615617	20000427

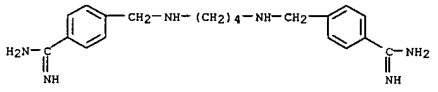
PRIORITY APPLN. INFO.: US 1999-131779P P 19990430
WO 2000-US11591 W 20000427

OTHER SOURCE(S): MARPAT 133:350095

IT **304911-05-5P**, SL 11137 **304911-11-3P**, SL 11134
304911-12-4P, SL 11136
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of conformationally restricted polyamines as antiproliferative prostate cancer agents)

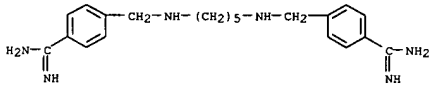
RN 304911-05-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



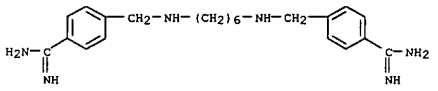
●4 HCl

RN 304911-11-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

RN 304911-12-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB The invention relates to peptide conjugates in which cytocidal and cytostatic agents, such as polyamine analogs or naphthoquinones, are conjugated to a polypeptide recognized and cleaved by enzymes such as prostate-specific antigen (PSA) and cathepsin B. Methods of using these conjugates in the treatment of prostate diseases are also provided. Thus, c2[CH2NH(CH2)4NHEt]2.4HCl (SL-11103), 4-[[7-[4-(9-acridinylamino)phenyl]heptyl]oxy]-1,2-naphthoquinone (SL-11064), and morpholino-Ser-Lys-Leu-Gln-.beta.-Ala-.beta.-lapachone (SL-11147) were prepd. and assayed for antitumor activity against human prostate cancer cell lines, such as PC-3 and DUPRO.

ACCESSION NUMBER: 2000:790358 CAPLUS
DOCUMENT NUMBER: 133:350515
TITLE: Preparation of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.
PATENT ASSIGNEE(S): Slil Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066175	A2	20001109	WO 2000-US11542	20000427
WO 2000066175	A3	20010802		
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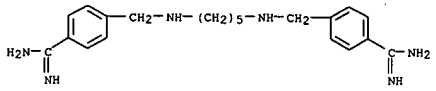
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173223	A2	20020123	EP 2000-928565	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010700	A	20020213	BR 2000-10700	20000427
JP 2002543163	T2	20021217	JP 2000-615058	20000427
PRIORITY APPLN. INFO.:			US 1999-131809P P	19990430
			WO 2000-US11542 W	20000427

OTHER SOURCE(S): MARPAT 133:350515

IT **304911-11-3P**, SL 11134 **304911-12-4P**, SL 11136
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)

RN 304911-11-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,5-pentanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

L12 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



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RN 304911-12-4 CAPLUS
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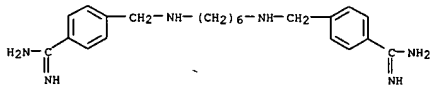

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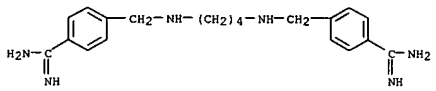
IT **304911-05-5P**, SL 11137
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)

RN 304911-05-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



●4 HCl

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FILE 'REGISTRY' ENTERED AT 16:32:04 ON 06 FEB 2003
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STRUCTURE FILE UPDATES:     5 FEB 2003  HIGHEST RN 486392-61-4
DICTIONARY FILE UPDATES:    5 FEB 2003  HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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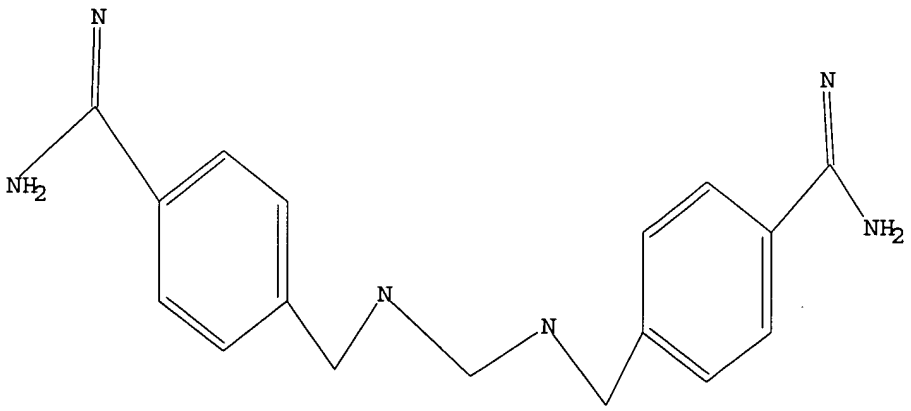


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Structure attributes must be viewed using STN Express query preparation.
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SAMPLE SCREEN SEARCH COMPLETED -      5 TO ITERATE

100.0% PROCESSED       5 ITERATIONS                                  0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            5 TO      234
PROJECTED ANSWERS:               0 TO        0

L14           0 SEA SSS SAM L13

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SEARCH TIME: 00.00.01

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L16             STR
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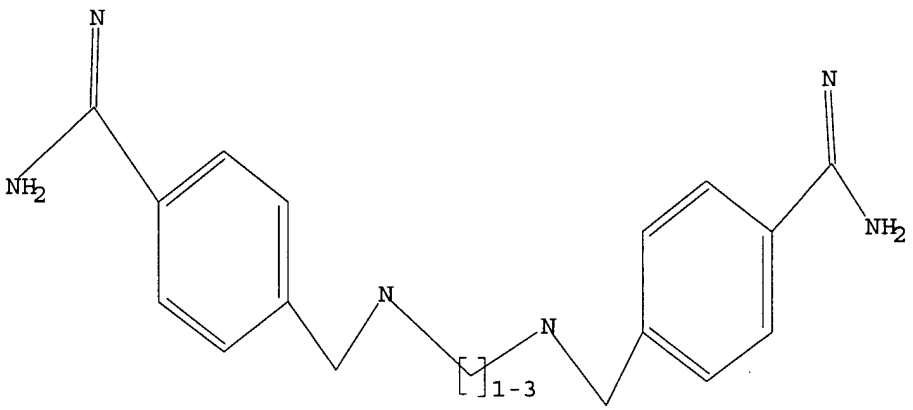


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                        BATCH   **COMPLETE**
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PROJECTED ANSWERS:               0 TO        0

L17           0 SEA SSS SAM L16

=> s l16 full
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SEARCH TIME: 00.00.01

L18           2 SEA SSS FUL L16

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FULL ESTIMATED COST                                   296.30     885.34

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -19.54

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FILE COVERS 1907 - 6 Feb 2003  VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003  (20030205/ED)

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=> s l18
L19           1 L18

=> d l19 abs ibib hitstr
```

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

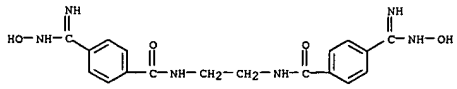
AB Arom. dicationic compds., such as pentamidine, have potent antimicrobial activities. Clin. use of these compds. has been restricted, however, by their toxicity and limited oral activity. A novel approach, using amidoxime derivs. as prodrugs, has recently been proposed to overcome these limitations. Although results were presented for amidoxime derivs. of only one diamidine, pentamidine, the authors in the original proposal claimed that amidoxime derivs. would work as effective prodrugs for all pharmacol. active diamidines. Nine novel amidoxime derivs. were synthesized and tested in the present study for activity against Pneumocystis carinii in corticosteroid-suppressed rats. Only three of the nine compds. had significant oral anti-Pneumocystis activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had excellent oral and i.v. activities and reduced acute host toxicity. These compds. are not likely candidates for future drug development, however, because they have chronic toxic effects and the active amidine compds. have multiple sites susceptible to oxidative metab., which complicates their pharmacol. and toxicol. Novel diamidoximes from three other structural classes, contg. different groups linking the cationic moieties, lacked significant oral or i.v. anti-Pneumocystis activity, even though the corresponding diamidines were very active i.v. Both active and inactive amidoximes were readily metabolized to the corresponding amidines by cell-free liver homogenates. Thus, the amidoxime prodrug approach may provide a strategy to exploit the potent antimicrobial and other pharmacol. activities of selected, but certainly not all, arom. diamidines.

ACCESSION NUMBER: 1998:189774 CAPLUS
DOCUMENT NUMBER: 128:303628
TITLE: Anti-Pneumocystis activities of aromatic diamidoxime prodrugs
AUTHOR(S): Hall, James Edwin; Kerrigan, John E.; Ramachandran, Kishore; Bender, Brendan C.; Stanko, Jason P.; Jones, Susan K.; Patrick, Donald A.; Tidwell, Richard R.
CORPORATE SOURCE: Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(3), 666-674
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **206532-31-2P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(anti-Pneumocystis activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)

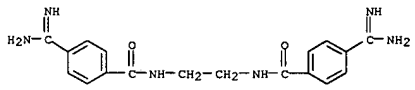
RN 206532-31-2 CAPLUS
CN Benzamide, N,N'-1,2-ethanediylbis[4-[(hydroxyamino)iminomethyl]- (9CI) (CA INDEX NAME)

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



IT **206532-32-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-Pneumocystis activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)

RN 206532-32-3 CAPLUS
CN Benzamide, N,N'-1,2-ethanediylbis[4-(aminoiminomethyl)- (9CI) (CA INDEX NAME)



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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         5.79     891.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                        -0.65     -20.19

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DICTIONARY FILE UPDATES:    5 FEB 2003  HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
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Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09560711.str

L20     STRUCTURE UPLOADED

=> d query
L20             STR
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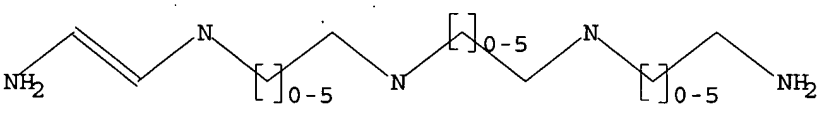


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Structure attributes must be viewed using STN Express query preparation.


=> s l20
SAMPLE SEARCH INITIATED 16:39:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   3553 TO ITERATE

 28.1% PROCESSED    1000 ITERATIONS                              0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        67487 TO    74633
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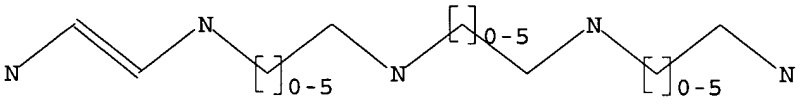
```
PROJECTED ANSWERS:                0 TO        0

L21            0 SEA SSS SAM L20

=> s l20 full
FULL SEARCH INITIATED 16:40:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  72286 TO ITERATE

100.0% PROCESSED   72286 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.02

L22            0 SEA SSS FUL L20

=>
Uploading 09560711.str

L23     STRUCTURE UPLOADED

=> d queyr
L23 HAS NO ANSWERS
'QUEYR ' IS NOT A VALID STRUCTURE FORMAT KEYWORD
Structure Formats
SIA ----- Structure Image, Attributes, and map table if it contains
          data.  (Default)
SIM ----- Structure IMage.
SAT ----- Structure ATtributes and map table if it contains data.
SCT ----- Structure Connection Table and map table if it contains
          data.
SDA ----- All Structure DAta (image, attributes, connection table and
          map table if it contains data).
NOS ----- NO Structure data.
ENTER STRUCTURE FORMAT (SIM), NOS:nos
L23             STR


=> d query
L23             STR
```

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Structure attributes must be viewed using STN Express query preparation.


=> s l23
SAMPLE SEARCH INITIATED 16:41:20 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   3553 TO ITERATE

 28.1% PROCESSED    1000 ITERATIONS                                0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        67487 TO    74633
PROJECTED ANSWERS:               0 TO        0
```

```
L24             0 SEA SSS SAM L23

=> s 23 full
L25      460971 23

=> s l23
SAMPLE SEARCH INITIATED 16:41:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    3553 TO ITERATE

 28.1% PROCESSED     1000 ITERATIONS                                 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        67487 TO    74633
PROJECTED ANSWERS:               0 TO        0

L26             0 SEA SSS SAM L23

=> s l23 full
FULL SEARCH INITIATED 16:41:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  72286 TO ITERATE

100.0% PROCESSED   72286 ITERATIONS                                 6 ANSWERS
SEARCH TIME: 00.00.01

L27             6 SEA SSS FUL L23

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   304.12    1195.25

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -20.19

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FILE COVERS 1907 - 6 Feb 2003  VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003  (20030205/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
```

```
=> s l27
L28             3 L27

=> d l28 1-3 abs ibib hitstr
```

L28 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
AB The possibility of electron binding by a mol. with two polar ends, each of
which is capable of electron binding, is studied using electronic structure methods. The destabilizing effects of each dipole on the ability of the other dipole to bind an electron as well as the through-bond splitting between the g and u anion states are examd. In addn., the ability of the two polar ends to bind two electrons, one to each end, is investigated. Numerical results are presented for the anions
of (HCN)n .cntdot..cntdot..cntdot. HCCH .cntdot..cntdot..cntdot. (NCH)n (n
= 2-4) and for the corresponding n = 2 dianion.

ACCESSION NUMBER: 2000:508846 CAPLUS
DOCUMENT NUMBER: 133:286775
TITLE: Bi-dipole-bound anions
AUTHOR(S): Gutowski, M.; Skurski, P.; Simons, J.
CORPORATE SOURCE: Materials Resources, Pacific Northwest National Laboratory, Richland, WA, 99352, USA
SOURCE: International Journal of Mass Spectrometry (2000), 201(1-3), 245-252
CODEN: IMSPF8; ISSN: 1387-3806
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **300347-22-2**
RL: PRP (Properties)
(electronic structure and electron attachment energy of)
RN 300347-22-2 CAPLUS
CN Methanimidamide, N',N'''-1,2-ethenediylbis[N-[[[(methyleneamino)methylene]amino]methylene]- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

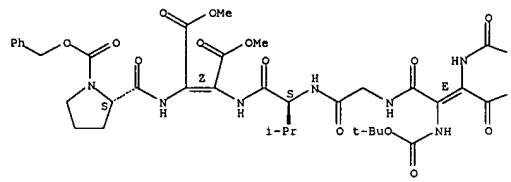
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS
AB Treatment of peptides contg. an .alpha.-(chloro)glycine residue with triethylamine and catalytic amts. of triphenylphosphine constitutes an efficient method for the stereoselective synthesis of amino acid and peptide dimers bridged by a C=C double bond. The dimers can be converted into novel peptide structures by std. methods of peptide synthesis.

ACCESSION NUMBER: 2000:447433 CAPLUS
DOCUMENT NUMBER: 133:208164
TITLE: Stereocontrolled backbone connection of peptides by C=C-double bonds
AUTHOR(S): Schumann, Susanne; Zeitler, Kirsten; Jager, Martin; Polborn, Kurt; Steglich, Wolfgang
CORPORATE SOURCE: Department Chemie der Ludwig-Maximilians-Universitat Munchen, Munchen, D-81377, Germany
SOURCE: Tetrahedron (2000), 56(25), 4187-4195
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:208164
IT **290346-38-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereocontrolled prepn. of a triple dimeric peptide linked via C=C double bonds)
RN 290346-38-2 CAPLUS
CN Aspartic acid, (2E)-2,3-didehydro-N-[(1,1-dimethylethoxy)carbonyl]-3-[[(1,1-dimethylethoxy)carbonyl]amino]aspartoylbis[glycyl-L-valyl-2,3-didehydro-3-[[[(2S)-1-[(phenylmethoxy)carbonyl]-2-pyrrolidinyl]carbonyl]amino]-, tetramethyl ester, [4(2Z),4'(2Z)]- (9CI) (CA INDEX NAME)

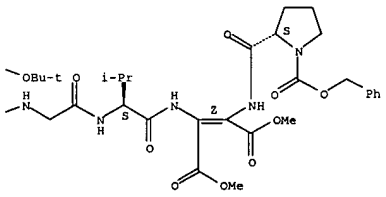
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



L28 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 1-B



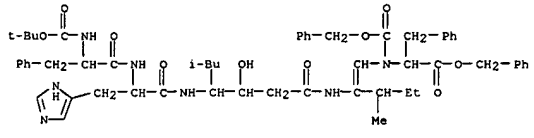
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AB RWW1NHCHR2CHR3CH2COR1 [I; R = H, acyl, (protected) Pro, pyroglutamyl; W = Phe, His, Leu, Tyr, 1-naphthylalanyl; W1 = Phe, His, Leu, Tyr, Nle; the N of the WW1 peptide link may be substituted by C1-4 alkyl when W = Phe and W1 = His; R2 = H, C1-6 alkyl, Ph, C4-7 cycloalkyl, C7-9 phenylalkyl, C5-10
cycloalkyl(alkylene); R3 = OH, amino, acylamino, alkoxy, alkoxycarbonyl; R1 = amino, C1-4 alkoxy, 4-benzylpiperazin-1-yl, 1,2,3,4-tetrahydroquinolin-1-yl, A-E-B, etc.; A = Lys, Pro, Ile; E = Phe, Gly, Ala, Val, Ile, Lys, Orn, Arg, Asp, etc.; B = OH, alkoxy, amino, glutamyl, etc.] and their salts were prepd. as renin inhibitors. BOC-Phe-His-Sta-Ile-Sta-OH (Sta = 4S-amino-3S-hydroxy-6-methylheptanoyl), prepd. by the soln. phase method, inhibited renin with an IC50 of <4 .mu.mol/L.

ACCESSION NUMBER: 1989:173764 CAPLUS
DOCUMENT NUMBER: 110:173764
TITLE: Preparation and testing of statine-containing peptides as renin inhibitors
INVENTOR(S): Bindra, Jasit S.; Kleinman, Edward F.; Rosati, Robert L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 763,768, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4749687	A	19880607	US 1986-839010	19860310
CA 1254699	A1	19890523	CA 1985-476191	19850311
PRIORITY APPLN. INFO.:			US 1984-588279	19840312
			CA 1985-476191	19850311
			US 1985-763768	19850808

OTHER SOURCE(S): MARPAT 110:173764
IT **118384-89-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrogenolysis of, in prepn. of renin inhibitor)
RN 118384-89-7 CAPLUS
CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[2-hydroxy-4-[[2-methyl-1-[[[2-oxo-2-(phenylmethoxy)-1-
(phenylmethyl)ethyl][(phenylmethoxy)carbonyl]amino]methylene]butyl]amino]-1-(2-methylpropyl)-4-oxobutyl]-, [1S-[1R*,2R*,4[R*(R*)]]]- (9CI) (CA INDEX NAME)



RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for renin inhibitor

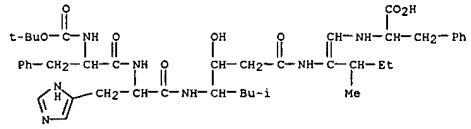
IT **118403-86-4P 118403-87-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)

RN 118403-86-4 CAPLUS

CN L-Histidinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[1-[[(1-carboxy-2-phenylethyl)amino]methylene]-2-methylbutyl]amino]-2-hydroxy-1-(2-methylpropyl)-4-oxobutyl]-, [1S-[1R*,2R*,4[R*(R*)]]]-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 118403-85-3
CMF C43 H61 N7 O8

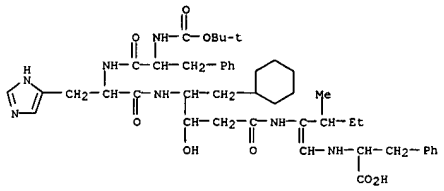


CM 2

CRN 64-19-7
CMF C2 H4 O2

RN 118403-87-5 CAPLUS

CN L-Phenylalanine, N-[2-[[5-cyclohexyl-2,4,5-trideoxy-4-[[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl]-L-histidyl]amino]-L-threo-pentonoyl]amino]-3-methyl-1-pentenyl]-, (S)- (9CI) (CA INDEX NAME)



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FULL ESTIMATED COST                                    14.03    1209.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -1.95     -22.14

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DICTIONARY FILE UPDATES:   5 FEB 2003  HIGHEST RN 486392-61-4

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PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     2.00    1211.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -22.14

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FILE COVERS 1907 - 6 Feb 2003  VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003  (20030205/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s polyamine
         28502 POLYAMINE
         29335 POLYAMINES
L29      40432 POLYAMINE
                (POLYAMINE OR POLYAMINES)

=> s conformation?
L30     294106 CONFORMATION?

=> s l29 and l30
L31        672 L29 AND L30

=> logoff y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     4.28    1215.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -22.14

STN INTERNATIONAL LOGOFF AT 16:46:58 ON 06 FEB 2003
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